(54) Title: PROTECTIVE PROTEIN/CATHEPSIN A AND PRECURSOR: CRYSTALLIZATION, X-RAY DIFFRACTION, THREE-DIMENSIONAL STRUCTURE DETERMINATION AND RATIONAL DRUG DESIGN

(57) Abstract

The present invention provides crystallized protective protein/cathepsin A (PPCA), a precursor thereof (pPPCA) or at least one subdomain thereof; methods for x-ray diffraction analysis to provide x-ray diffraction patterns of sufficiently high resolution for three-dimensional structure determination of the protein, as well as methods for rational drug design (RDD), based on using amino acid sequence data and/or x-ray crystallography data provided on computer readable media, as analyzed on a computer system having suitable computer algorithms.

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Protective Protein/Cathepsin A and Precursor: Crystallization, X-Ray Diffraction, Three-Dimensional Structure Determination and Rational Drug Design

Background of the Invention

5 *Statement as to Rights to Inventions Made Under*
Federally-Sponsored Research and Development

Part of the work performed during development of this invention utilized U.S. Government funds. The U.S. Government has certain rights in this invention.

Field of the Invention

10 The present invention is in the fields of molecular biology, protein purification, protein crystallization, x-ray diffraction analysis, three-dimensional structure determination and rational drug design (RDD). The present invention provides crystallized protective protein/cathepsin A (PPCA) and its precursor (pPPCA). The crystallized PPCA or pPPCA is analyzed by x-ray diffraction techniques. The resulting x-ray diffraction patterns are of sufficiently high resolution to be useful for determining the three-dimensional structure of the PPCA or pPPCA protein, and for RDD.

15 *Related Background Art*

The human protective protein/cathepsin A (PPCA, also known as human protective protein or HPP) has been identified as the primary genetic defect underlying galactosialidosis (d'Azzo *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* 79:4535-4539 (1982)), a lysosomal storage disease inherited as an autosomal recessive trait. Patients with this disorder are diagnosed as having drastically reduced β-galactosidase and neuraminidase activities in their cell lysosomes. Examples

20 of lysosomal storage diseases are presented in Table 316-1 of Braunwald *et al.*, eds., *Harrison's Principles of Internal Medicine*, 11th Ed., pp. 1661-1671, McGraw Hill Book Co., New York (1987); as well as Wenger *et al.*, *Biochem. Biophys. Res. Commun.* 82:589-595 (1978); Tettamanti *et al.* eds., *Sialidases and Sialidosis. Perspectives in Inherited Metabolic Diseases*. Vol. 4, Edi. Ermes, Milano (1981), pp. 261-279 and 379-395; and van Diggelen *et. al. Lancet* 2:804(1987), which references are entirely incorporated herein by reference..

25 Researchers have proposed that one of PPCA's functions is to stabilize β-galactosidase and neuraminidase in a multi-enzyme complex, which complex is deficient in galactosialidosis patients (d'Azzo *et al.* (1982), *infra*; Hoogeveen *et al.* (1983), *infra*). Evidence for this protective function comes from studies showing that PPCA is taken up from the culture medium by galactosialidosis fibroblasts and that PPCA restores both β-galactosidase and neuraminidase activities to these fibroblasts (d'Azzo *et al.* (1982), *infra*).

30 The cDNA for PPCA directs the synthesis of a 452 amino acid precursor PPCA (pPPCA) (Figure 13) with a molecular weight of 54 kDa (Galjart *et al.*, *Cell.* 54:755-764 (1988)). The amino acid sequences of PPCA (Figure 14) and pPPCA (Figure 13) contain two glycosylation sites (Asn 117 and Asn 305), both of which are glycosylated in cultured fibroblasts and cells over-expressing PPCA or pPPCA. pPPCA dimerizes soon after synthesis in the endoplasmic reticulum (ER) (Zhou *et al.*, *EMBO J.* 10:404-4048 (1991)).

35 Lysosomal PPCA has cathepsin A/deamidase/esterase activities which are exerted *in vitro* on a specific subset of bioactive peptides. Non-limiting examples of those hydrolyzed by PPCA are: substance P and substance P-free acid; oxytocin and oxytocin-free acid; neurokinin A; angiotensin I; bradykinin (Jackman *infra*. (1990). Furthermore, the enzyme inactivates endothelin I activity in rat smooth muscle cells and normal human tissues. This activity was deficient in liver from a galactosialidosis patient (Itoh, *infra*. 1995; Jackman *et al.*, *J. Biol. Chem.* 267:2872-2875, (1992).

40 Endothelins (ET-1, ET-2 and ET-3) are potent vasoconstrictors and elevate blood pressure in mammals. They also influence cell proliferation and hormone production and have been implicated in cardiovascular disorders, ranging from hypertension to stroke to ischemic heart disease (Rubanyi and Polokoff, *Pharmc.Rev.* 46:325-415 (1994)).

The three-dimensional structure of a PPCA or a pPPCA has not previously been published, which structure could delineate specific biological activities and ligands as therapeutics for PPCA-related pathologies. Accordingly,

45 there is a need to provide three-dimensional structures of at least one PPCA, pPPCA or ligands for diagnosis or therapy of PPCA-related pathologies.

Summary of the Invention

The present invention provides methods of expressing, purifying and crystallizing a human protective protein/cathepsin A (PPCA) and its precursor, precursor protective protein/cathepsin A (pPPCA). The present invention also provides methods for obtaining crystallized PPCA or pPPCA that can be analyzed to obtain x-ray diffraction patterns of sufficiently high resolution to be useful for three-dimensional structure determination of the protein.

The x-ray diffraction patterns can be either analyzed directly to provide the three dimensional structure (if of sufficiently by high resolution), or atomic coordinates for the crystallized PPCA or pPPCA, as provided herein, can be used for structure determination. The x-ray pattern/diffraction patterns obtained by methods of the present invention, and provided on computer readable media, are used to provide electron density maps. The amino acid sequence is also useful for three-dimensional structure determination. The data is then used in combination with phase determination (e.g., using multiple isomorphous replacement (MIR) molecular replacement techniques) to generate electron density maps of a PPCA or a pPPCA, using a suitable computer system.

The electron density maps, provided by analysis of either the x-ray diffraction patterns or working backwards from the atomic coordinates, provided herein, are then fitted using suitable computer algorithms to generate secondary, tertiary and/or quaternary domains of a PPCA or a pPPCA, which domains are then used to provide an overall three-dimensional structure, as well as expected binding and active sites of the PPCA or pPPCA. pPPCA has some of the active and binding sites of PPCA, except for changes in structure due to the presence of the portion of the pPPCA which is deleted during maturation to PPCA (e.g., residues 285-298 of Figure 13).

Structure determination methods and computer systems are also provided by the present invention for rational drug design (RDD). These RDD methods use computer modeling programs to find potential ligands that are calculated to associate with, or bind to, sites or domains of a PPCA or a pPPCA. Potential ligands are then screened for modulating or binding activity. Such screening methods can be selected from assays for at least one PPCA-specific structural feature or biological activity, preferably as associated with a PPCA- or pPPCA-related pathology, e.g., protective activity (e.g., modulation of β-galactosidase activity and neuraminidase (NA) activity); and peptide or enzyme modulating activity (e.g., of endothelin I (serine carboxypeptidase), neuropeptides, cathepsin A, and the like), according to known assays. The resulting ligands provided by methods of the present invention are synthesized and are useful for treating, inhibiting or preventing at least one of PPCA related pathology in a mammal.

Other objects of the invention will be apparent to one of ordinary skill in the art from the following detailed description and examples relating to the present invention.

Brief Description of the Figures

Figure 1: is a schematic ribbon diagram of the PPCA monomer (monomer 1), where Secondary structure assignments are according to DSSP (Kabsch and Sander, Biopolymers 22:2577-2637 (1983)). The 'core' domain is shown in yellow. The 'cap' domain consists of a 'helical' subdomain, in red, and a 'maturation' subdomain, in orange. The catalytic triad Ser 150, His 429 and Asp 372 (from right to left) is shown by small green spheres. (Figure generated using MOLSCRIPT (Kraulis, J. Appl. Cryst. 24:946-950 (1991))).

Figure 2 is stereo diagram is presented of the C^α, trace of the PPCA monomer 1 with numbering of selected residues. The residues forming the α-helices and β-strands are as follows according to DSSP:

Core domain: Cβ1 (21-27); Cβ2(32-39); Cβ3(50-54); Cα1(63-67) Cβ4(73-75); Cβ5(82-84); Cβ6(94-98); Cα2(118-135); Cβ7(144-149); Cα3(152-163); Cβ8(171-177); Cα4(307-313); Cα5(316-321); Cα6(336-341); Cα7(350-359); Cβ9(363-369); Cα8(377-386); Cβ10(391-401); Cβ11(407-416); Cβ12(419-424); Cα9(431-434); Cα10(436-447);

Cap domain: Hα1(183-196); Hα2(202-212); Hα3(226-240); Mβ1(261-264); Mβ2(267-270); Mα1(290-293); Mβ3(296-299). Note that for monomer 2 the secondary structure assignments in the cap domain are slightly different than in monomer 1. Residues in Hβ1 are in a region of poor density and Mα1 is an extended coil. (Figure generated using MOLSCRIPT (Kraulis (1991). infra).

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Figure 3 shows the density for the disulfide bridges Cys 212-Cys 228 and Cys 213-Cys 218 is presented as revealed in the SigmaA weighted 2mF$_0$-DF$_c$ electron density map (Read, *Acta Crystallogr. A 42*:140-149 (1986)) calculated from the model refined to 2.2 Å; the map has been contoured at 1σ. (Figure drawn with the O computer program (Jones, *Acta Crystallogr. A47*:110-119 (1991))).

Figure 4 is stereo diagram is presented of the superimposed C^α traces from the two crystallographically independent PPCA monomers forming the dimer. Monomer 1 is in blue, monomer 2 is in red. Residues referred to in the text are labeled. Residues 259 and 260 have not been incorporated in the model of monomer 2, since no electron density was observed for them. Note the tremendous difference in conformation of the excision peptide located in the upper right corner of the proteins. (Figure generated by MOLSCRIPT (Kraulis (1991), *infra*)).

Figure 5 is a schematic ribbon diagram is presented of the PPCA dimer viewed approximately along the two-fold axis. For monomer 1, the core domain is yellow while the cap domain consists of a helical subdomain in red and a maturation subdomain in orange. For monomer 2, the core domain is green, while the cap domain consists of a blue helical subdomain and a light blue maturation subdomain. (Figure generated using MOLSCRIPT (Kraulis (1991), *infra*)).

Figure 6A-B is a representation of the molecular surface of the PPCA dimer. The surface was calculated with GRASP (Nicholls, A., *et al., Proteins 11*:281-296 (1991)) and colored according to the electrostatic potential. Dark blue corresponds to positive potential > + 15.0 kT/e and dark red to a negative <-15.0 kT/e potential. Figure 6A: standard view, along the diad with the dimer oriented as in Figure 4. Figure 6B: side view of the dimer, ninety degrees rotated with respect to 6A.

Figure 7A-F presents a topological comparison of 6 members of the hydrolase fold family. The arrangement of structural elements in the central core domain (in green and yellow) of the different proteins is generally similar. The cap domains (in red) vary greatly. The following structures are shown starting from the top left hand corner (references and PDB entry codes are given in between brackets): Figure 7A shows the PPCA precursor cap domain that consists of two subdomains one α-helical and the other mainly β-sheet; Figure 7B shows CPW (3SC2, Liao *et al.* (1992) *infra*), cap domain helical; Figure 7C shows CPY (LYSC, Endrizzi *et al.* (1994), *infra*), cap domain helical; Figure 7D shows dehalogenase (2HAD, Franken *et al., J. EMBO 10*:1297-1302 (1991)), cap domain helical but quite different from the serine carboxypeptidases; Figure 7E shows lipase from *Pseudomonas glumae* (1TAH, Noble *et al., FEBS Lett. 331*:123-128 (1993)), cap domain mixed α-helical and β-strands; and Figure 7F shows acetylcholine esterase (1ACE, Sussman *et al., Science 253*: 872-879 (1991)), cap domain large and predominantly α-helical. The secondary structure assignments were generated with the computer program O, using structures provided and/or available from the Brookhaven Protein Data Bank. (This Figure was generated using MOLSCRIPT (Kraulis (1991), *infra*)).

Figure 8A-B shows the superposition of the C^α traces from the PPCA and CPW monomers, showing that the major differences between the two enzymes are localized in the cap domain. PPCA has a large 'maturation' subdomain and the 'helical subdomain' is rotated with respect to the CPW counterpart (Figure drawn with the O program (Jones (1991), *infra*)). Figure 8B shows the C^α traces from the PPCA and CPW dimers after the core domains from the subunits (shown on the right hand side of the two dimers) have been superimposed. Notice the remarkable difference in mutual orientation (of 15°) of the two subunits on the left hand side of the two dimers, which has been accentuated by an arrow. (Figure drawn with the O computer program (Jones (1991), *supra*)).

Figure 9 is a stereo view of the Ca trace of PPCA monomer 1 highlighting regions involved in the maturation event. Color scheme for the trace is as follows: core domain in light blue, helical subdomain in red, maturation subdomain in orange with the exception of the excision peptide (residues 285-298) which is shown in blue. Orange sphere mark the residues 272 and 277 marking the beginning and end of the blocking peptide. The catalytic triad Ser 150, His 429 and Asp 372 is shown as light blue spheres. Two cysteines Cys 253 and Cys 303 referred to in the discussion are colored green. (This Figure generated using MOLSCRIPT (Kraulis (1991), *infra*)).

Figure 10 is a close-up representation of the 'blocking' peptide (residues 272-277) bound in the active site, rendering the catalytic triad solvent inaccessible. Residues from the maturation subdomain are shown in orange, residues

from the helical domain in magenta and residues from the core domain in cyan. The excision peptide is shown in blue. Side chains are shown for residues making extensive contacts with the blocking peptide or if mentioned in the text. The catalytic triad is shown in white. (Figure drawn with O (Jones (1991), *infra*)).

Figure 11 is a representation of elements proposed to be involved in the activation mechanism of the precursor form of PPCA as discussed in the text. The Cᵃ-trace of the core domain is shown in cyan, the helical subdomain in red, the maturation subdomain in orange, and the excision peptide is shown in blue. Relevant side chains are depicted and labeled. Rearrangement of the residues 254-302 limited by the disulfide Cys 253 and Cys 303 would free up the active site cleft. A charge cluster Arg 262, Glu 264, Arg 298 and Asp 300 occupies a strategic position within the maturation subdomain, possibly involved in pH dependent regulation of conformational changes. The solvent accessible surface was calculated and visualized with the atomic coordinates by BIOGRAF (BIOGRAF Construct Users Guide Version 3.2.1., June 1993).

Figure 12 is a schematic representation of the proposed activation of PPCA. The active site cleft is formed by the core domain (indicated as 'core' in the above scheme) and the helical subdomain (indicated as 'α'). The maturation subdomain (indicated as 'm') contains the residues that block the active site cleft rendering the precursor enzymatically inactive, shown in structure 1. In the acidic endosome/lysosome, the precursor undergoes activation. In activation pathway 2a, conformational rearrangements induced by low pH might render the excision peptide more accessible to proteases as a first step, followed by cleavage of the polypeptide chain removing the excision peptide. Alternatively, in pathway 2b, proteolytic cleavage of the excision peptide might form the trigger for the total rearrangement, removing the blocking peptide from the active site and thus generating the fully active enzyme as shown in structure 3.

Figure 13 shows the amino acid sequence of a human pPPCA. The underlined portion (residues 285-298) shows an excision peptide for conversion to the mature form, PPCA.

Figure 14 shows the amino acid sequence of a human PPCA.

Figure 15 shows a sequence alignment between pPPCA, CPW and CPY (top three sequences shown). Identical residues among all three sequences are boxed. Residue numbering is included for the pPPCA amino acid sequence. The alignment was made using the GCG program PILEUP (GCG version 8), then manually adjusted using 3D-structural knowledge from the superposition of the CPW (Liao *et al.*, 1992) and CPY (Endrizzi *et al.*, 1994) atomic coordinates. The alignment was later used to design a multi-Ala search probe for molecular replacement calculations shown in the fourth sequence shown as 'model'. The structure determination of pPPCA subsequently revealed that the protein can be divided in two domains: a 'core' domain (residues 1-182 and 303-452) and 'cap' domain (residues 183-302). The secondary structure elements for the PPCA precursor are depicted with shaded bars (for details on the assignment and nomenclature, see Rudenko *et al. Structure* 3:1249-1259 (1988)).

Figure 16 shows a schematic representation of a 'bootstrapping' cycle as described in Example 2.

Figure 17 is a representation of an initial molecular mask enlarged to accommodate missing area's in the model. The program MAMA (Kleywegt & Jones, 1994) was used to calculate the mask and mask editing options in O (Jones *et al.*, 1991) were used to extend the mask.

Figure 18 is a representation of an enlargement of the model during the bootstrapping procedure plotted as a function of the expansion step. The number of Cᵃ atoms incorporated in the model per monomer is given (—o—) as well as the number of correct side chains (—●—). Note that after the first round of building in the molecular replacement map (expansion step 'mr'). 37 residues from the molecular replacement search probes had to be deleted from the model reducing the number of Cᵃ atoms to 294. Subsequent cycles allowed for the model to be expanded by small increments.

Figure 19 is a representation of a comparison of the Cᵃ trace from a monomer core model (shown in magenta) and the complete PPCA monomer (shown in yellow). The core model contained only 294 Cᵃ atoms. The 452 residue PPCA monomer consists of a core domain and a cap domain. The helical subdomain and the maturation subdomain forming the cap domain have been shown in the figure above.

Figure 20A-D is a representation of the resolving power of the bootstrapping procedure showing three different stages in map quality. The atomic coordinates of the refined model are visualized with the electron density in Figures 20B. 20C and 20D. Figures 20A and 20B show the initial $2m|F_{obs}|-D|F_{calc}|$ SigmaA weighted map calculated using phases from the molecular replacement solution. The electron density is essentially uninterpretable. Fig. 20C shows twofold averaged $2|F_{obs}|-|F_{inv}|$ electron density map calculated using inverted phases from cycle bmc6. The density for β-strand Mβ2 (residues 266-271) has become clearly visible. Fig. 20D shows unaveraged $2m|F_{obs}|-D|F_{calc}|$ SigmaA weighted map calculated using phases from the refined model. The quality of the density is very good. Density for the helix Mα1 (residues 287-293) which assumes a different conformation in the two monomers is now also apparent.

Figure 21 shows a Ramachandran plot calculated for one monomer from a refined model of a pPPCA. Both monomers in the asymmetric unit give essentially equivalent plots.

Figure 22 shows a schematic of a computer system for PPCA or pPPCA structure determination and/or rational drug design.

Figure 23.1-52 lists the atomic coordinates for the active site of a pPPCA dimer having the amino acid sequence presented as portions of at least one of 50-76, 144-155, 173-197, 226-253, 226-288, 294-310, 327-344, 338-350, 366-381 and 423-436 of (Figure 23.1-23.26) 452 amino acids (designated 1-452) of monomer 1, as well as corresponding portions of (Figure 23.26-23.52) 452 amino acids (designated 1001-1452) of monomer 2.

Detailed Description of the Preferred Embodiments

The present invention provides methods for expressing. purifying and crystallizing a protective protein/cathepsin A (PPCA) or a precursor protective protein/cathepsin A (pPPCA), where the crystals diffract x-rays with sufficiently high resolution to allow determination of the three-dimensional structure of the PPCA or pPPCA, or a portion or subdomain thereof. The three-dimensional structure (e.g.,as provided on computer readable media of the present invention) is useful for rational drug design of ligands of a PPCA or a pPPCA. Such ligands can be synthesized or recombinantly produced and are useful as diagnostic agents or drugs for diagnosing, treating, inhibiting or preventing at least one PPCA- or pPPCA-related pathology.

The determined structure is made using the PPCA or pPPCA amino acid sequences and/or atomic coordinate/x-ray diffraction data. which are analyzed to provide atomic model output data corresponding to the three-dimensional structure, e.g., as provided on computer readable media. The computer analysis of the atomic coordinate/x-ray diffraction data and/or the amino acid sequence allows the calculation of the secondary, tertiary and/or quaternary structures; domains; and/or subdomains of the protein. These domains are combined and refined by additional calculations using suitable computer subroutines to determine the most probable or actual three-dimensional structure of the PPCA or pPPCA, including potential or actual active sites, binding sites or other structural or functional domains or subdomains of the protein.

Structure determination methods are also provided by the present invention for rational drug design (RDD) of PPCA or pPPCA ligands. Such drug design uses computer modeling programs that calculate different molecules expected to interact with the determined active sites. binding sites, or other structural or functional domains or subdomains of a PPCA or a pPPCA. These ligands can then be produced and screened for activity in modulating or binding to a PPCA or pPPCA, according to methods and compositions of the present invention.

The actual PPCA or pPPCA-ligand complexes can optionally be crystallized and analyzed using x-ray diffraction techniques. The diffraction patterns obtained are similarly used to calculate the three-dimensional interaction of the ligand and the PPCA or pPPCA, to confirm that the ligand binds to. or changes the conformation of, particular domain(s) or subdomain(s) of the PPCA or pPPCA. Such screening methods are selected from assays for at least one biological activity of a PPCA or a pPPCA. The resulting ligands. provided by methods of the present invention, modulate or bind at least one PPCA or pPPCA and are useful for diagnosing. treating or preventing PPCA- or pPPCA-related pathologies in animals. such as humans. Ligands of a particular PPCA or pPPCA can similarly modulate other PPCAs or pPPCAs from other sources. such as other eukaryotes.

A PPCA or pPPCA is also provided as a crystallized protein suitable for x-ray diffraction analysis. The x-ray diffraction patterns obtained by the x-ray analysis are of moderate, to moderately high, to high resolution, e.g., 30-10, 10-3.5 or 1.5-3.5 Å, respectively, with the higher resolutions included. These diffraction patterns are suitable and useful for three-dimensional structure determination of a PPCA or a pPPCA, domain or subdomain thereof.

5   The determination of the three-dimensional structure of a PPCA or pPPCA has a broad-based utility. Significant sequence identity and conservation of important structural elements are expected to exist among different PPCAs or pPPCAs. Therefore, the three-dimensional structure from one or few PPCAs or pPPCAs can be used to identify ligands that have diagnostic or therapeutic value for at least one PPCA- or pPPCA-related pathology that may involve PPCAs or pPPCAs having different amino acid sequences.

10   *Determination of Protein Structures*

Different techniques give different and complementary information about protein structure. The primary structure is obtained by biochemical methods, either by direct determination of the amino acid sequence from the protein, or from the nucleotide sequence of the corresponding gene or cDNA. The quaternary structure of large proteins or aggregates can also be determined by electron microscopy. To obtain the secondary and tertiary structure, which

15   requires detailed information about the arrangement of atoms within a protein, x-ray crystallography is preferred. *See, e.g.*, Blundell, *infra*; Oxender, *infra*; McPherson, *infra*; Wyckoff, *infra*.

The first prerequisite for solving the three-dimensional structure of a protein by x-ray crystallography is a well-ordered crystal that will diffract x-rays strongly. The crystallographic method directs a beam of x-rays onto a regular, repeating array of many identical molecules so that the x-rays are diffracted from it in a pattern from which the structure

20   of an individual molecule can be retrieved. Well-ordered crystals of globular protein molecules are large, spherical, or ellipsoidal objects with irregular surfaces, and crystals thereof contain large holes or channels that are formed between the individual molecules. These channels, which usually occupy more than half the volume of the crystal, are filled with disordered solvent molecules. The protein molecules are in contact with each other at only a few small regions. This is one reason why structures of proteins determined by x-ray crystallography are generally the same as those for the

25   proteins in solution.

The formation of crystals is dependent on a number of different parameters, including pH, temperature, protein concentration, the nature of the solvent and precipitant, as well as the presence of added ions or ligands to the protein. Many routine crystallization experiments may be needed to screen all these parameters for the few combinations that might give crystal suitable for x-ray diffraction analysis. Crystallization robots can automate and speed up the work of

30   reproducibly setting up large numbers of crystallization experiments.

A pure and homogeneous protein sample is important for successful crystallization. Proteins obtained from cloned genes in efficient expression vectors can be purified quickly to homogeneity in large quantities in a few purification steps. A protein to be crystallized is preferably at least 93-99% pure according to standard criteria of homogeneity. Crystals form when molecules are precipitated very slowly from supersaturated solutions. The most

35   frequently used procedure for making protein crystals is the hanging-drop method, in which a drop of protein solution is brought very gradually to supersaturation by loss of water from the droplet to the larger reservoir that contains salt or polyethylene glycol solution.

Different crystal forms can be more or less well-ordered and hence give diffraction patterns of different quality. As a general rule, the more closely the protein molecules pack, and consequently the less water the crystals contain, the

40   better is the diffraction pattern because the molecules are better ordered in the crystal.

X-rays are electromagnetic radiation at short wavelengths, emitted when electrons jump from a higher to a lower energy state. In conventional sources in the laboratory, x-rays are produced by high-voltage tubes in which a metal plate, the anode, is bombarded with accelerating electrons and thereby caused to emit x-rays of a specific wavelength, so-called monochromatic x-rays. The high voltage rapidly heats up the metal plate, which therefore has

to be cooled. Efficient cooling is achieved by so-called rotating anode x-ray generators, where the metal plate revolves during the experiment so that different parts are heated up.

More powerful x-ray beams can be produced in synchrotron storage rings where electrons (or positrons) travel close to the speed of light. These particles emit very strong radiation at all wavelengths from short gamma rays to visible
5   light. When used as an x-ray source, only radiation within a window of suitable wavelengths is channeled from the storage ring. Polychromatic x-ray beams are produced by having a broad window that allows through x-ray radiation with wavelengths of 0.2 - 3.5 Å.

In diffraction experiments a narrow and parallel beam of x-rays is taken out from the x-ray source and directed onto the crystal to produce diffracted beams. The incident primary beam causes damage to both protein and solvent
10   molecules. The crystal is, therefore, usually cooled to prolong its lifetime (e.g., -220 to -50°C). The primary beam must strike the crystal from many different directions to produce all possible diffraction spots, and so the crystal is rotated in the beam during the experiment.

The diffracted spots are recorded either on a film, the classical method, or by an electronic detector. The exposed film has to be measured and digitized by a scanning device, whereas electronic detectors feed the signals they
15   detect directly in a digitized form into a computer. Electronic area detectors (an electronic film) significantly reduce the time required to collect and measure diffraction data.

When the primary beam from an x-ray source strikes the crystal, some of the x-rays interact with the electrons on each atom and cause them to oscillate. The oscillating electrons serve as a new source of x-rays, which are emitted in almost all directions, referred to as scattering. When atoms (and hence their electrons) are arranged in a regular three-
20   dimensional array, as in a crystal, the x-rays emitted from the oscillating electrons interfere with one another. In most cases, these x-rays, colliding from different directions, cancel each other out; those from certain directions, however, will add together to produce diffracted beams of radiation that can be recorded as a pattern on a photographic plate or detector.

The diffraction pattern obtained in an x-ray experiment is related to the crystal that caused the diffraction. X-
25   rays that are reflected from adjacent planes travel different distances, and diffraction only occurs when the difference in distance is equal to the wavelength of the x-ray beam. This distance is dependent on the reflection angle, which is equal to the angle between the primary beam and the planes.

The relationship between the reflection angle (θ), the distance between the planes (d), and the wavelength (λ) is given by Bragg's law: $2d \sin \theta = \lambda$. This relation can be used to determine the size of the unit cell in the crystal.
30   Briefly, the position on the film of the diffraction data relates each spot to a specific set of planes through the crystal. By using Bragg's law, these positions can be used to determine the size of the unit cell.

Each atom in a crystal scatters x-rays in all directions, and only those that positively interfere with one another, according to Bragg's law, give rise to diffracted beams that can be recorded as a distinct diffraction spot above background. Each diffraction spot is the result of interference of all x-rays with the same diffraction angle emerging
35   from all atoms. For example, for the protein crystal of myoglobin, each of the about 20,000 diffracted beams that have been measured contain scattered x-rays from each of the around 1500 atoms in the molecule. To extract information about individual atoms from such a system requires considerable computation. The mathematical tool that is used to handle such problems is called the Fourier transform.

Each diffracted beam, which is recorded as a spot on the film, is defined by three properties: the amplitude,
40   which we can measure from the intensity of the spot; the wavelength, which is set by the x-ray source; and the phase, which is lost in x-ray experiments. All three properties are needed for all of the diffracted beams, in order to determine the position of the atoms giving rise to the diffracted beams.

For larger molecules, protein crystallographers have determined the phases in many cases using a method called multiple isomorphous replacement (MIR) (including heavy metal scattering), which requires the introduction of new
45   x-ray scatterers into the unit cell of the crystal. These additions are usually heavy atoms (so that they make a significant

contribution to the diffraction pattern), such that there should not be too many of them (so that their positions can be located); and they should not change the structure of the molecule or of the crystal cell, *i.e.*, the crystals should be isomorphous. Isomorphous replacement is usually done by diffusing different heavy-metal complexes into the channels of the preformed protein crystals. The protein molecules expose side chains (such as SH groups) into these solvent channels that are able to bind heavy metals. It is also possible to replace endogenous light metals in metalloproteins with heavier ones, *e.g.*, zinc by mercury, or calcium by samarium.

Since such heavy metals contain many more electrons than the light atoms (H, N, C, O, and S) of the protein, they scatter x-rays more strongly. All diffracted beams would therefore increase in intensity after heavy-metal substitution if all interference were positive. In fact, however, some interference is negative; consequently, following heavy-metal substitution, some spots measurably increase in intensity, others decrease, and many show no detectable difference.

Phase differences between diffracted spots can be determined from intensity changes following heavy-metal substitution. First, the intensity differences are used to deduce the positions of the heavy atoms in the crystal unit cell. Fourier summations of these intensity differences give maps of the vectors between the heavy atoms, the so-called Patterson maps. From these vector maps the atomic arrangement of the heavy atoms is deduced. From the positions of the heavy metals in the unit cell, one can calculate the amplitudes and phases of their contribution to the diffracted beams of protein crystals containing heavy metals.

This knowledge is then used to find the phase of the contribution from the protein in the absence of the heavy-metal atoms. As both the phase and amplitude of the heavy metals and the amplitude of the protein alone is known, as well as the amplitude of the protein plus heavy metals (*i.e.*, protein heavy-metal complex), one phase and three amplitudes are known. From this, the interference of the x-rays scattered by the heavy metals and protein can be calculated to see if it is constructive or destructive. The extent of positive or negative interference, with knowledge of the phase of the heavy metal, give an estimate of the phase of the protein. Because two different phase angles are determined and are equally good solutions, a second heavy-metal complex can be used which also gives two possible phase angles. Only one of these will have the same value as one of the two previous phase angles; it therefore represents the correct phase angle. In practice, more than two different heavy-metal complexes are usually made in order to give a reasonably good phase determination for all reflections. Each individual phase estimate contains experimental errors arising from errors in the measured amplitudes. Furthermore, for many reflections, the intensity differences are too small to measure after one particular isomorphous replacement, and others can be tried.

The amplitudes and the phases of the diffraction data from the protein crystals are used to calculate an electron-density map of the repeating unit of the crystal. This map then has to be interpreted as a polypeptide chain with a particular amino acid sequence. The interpretation of the electron-density map is made more complex by several limitations of the data. First of all, the map itself contains errors, mainly due to errors in the phase angles. In addition, the quality of the map depends on the resolution of the diffraction data, which in turn depends on how well-ordered the crystals are. This directly influences the image that can be produced. The resolution is measured in Å units: the smaller this number is, the higher the resolution and therefore the greater the amount of detail that can be seen.

Building the initial model is a trial-and-error process. First, one has to decide how the polypeptide chain weaves its way through the electron-density map. The resulting chain trace constitutes a hypothesis, by which one tries to match the density of the side chains to the known sequence of the polypeptide. When a reasonable chain trace has finally been obtained, an initial model is built to give the best fit of the atoms to the electron density. Computer graphics are used both for chain tracing and for model building to present the data and manipulated the models.

The initial model will contain some errors. Provided the protein crystals diffract to high enough resolution (*e.g.*, better than 3.5 Å), most or substantially all of the errors can be removed by crystallographic refinement of the model using computer algorithms. In this process, the model is changed to minimize the difference between the experimentally observed diffraction amplitudes and those calculated for a hypothetical crystal containing the model (instead of the real

molecule). This difference is expressed as an R factor (residual disagreement) which is 0.0 for exact agreement and about 0.59 for total disagreement.

In general, the R factor is preferably between 0.15 and 0.35 (such as less than about 0.24-0.28) for a well-determined protein structure. The residual difference is a consequence of errors and imperfections in the data. These derive from various sources, including slight variations in the conformation of the protein molecules, as well as inaccurate corrections both for the presence of solvent and for differences in the orientation of the microcrystals from which the crystal is built. This means that the final model represents an average of molecules that are slightly different both in conformation and orientation.

In refined structures at high resolution, there are usually no major errors in the orientation of individual residues. and the estimated errors in atomic positions are usually around 0.1-0.2 Å, provided the amino acid sequence is known. Hydrogen bonds, both within the protein and to bound ligands, can be identified with a high degree of confidence.

Most x-ray structures are determined to a resolution between 1.7 Å and 3.5 Å. Electron-density maps with this resolution range are preferably interpreted by fitting the known amino acid sequences into regions of electron density in which individual atoms are not resolved.

An amino acid sequence is preferred for accurate x-ray structure determination. Thus, recombinant DNA techniques have had a double impact on x-ray structural work. When a protein is cloned and overexpressed for structural studies. the amino acid sequence, necessary for the x-ray work, is also quickly obtained via the nucleotide sequence. Recombinant DNA techniques give us not only abundant supplies of rare proteins, but also their amino acid sequence as a bonus. *See, e.g..* Blundell. *infra*; Oxender, *infra*; McPherson, *infra*; Wyckoff, *infra*.

Isolated PPCA and pPPCA Polypeptides

A PPCA or pPPCA polypeptide can refer to any subset of a PPCA or pPPCA as a domain, subdomain, fragment, consensus sequence or repeating unit thereof. A PPCA or pPPCA polypeptide of the present invention can be prepared by, *e.g..*:

(a) recombinant DNA methods;

(b) proteolytic digestion of the intact molecule or a domain, subdomain or fragment thereof;

(c) chemical peptide synthesis methods well-known in the art; and/or

(d) by any other method capable of producing a PPCA or pPPCA polypeptide and having a conformation similar to a structural or functional subdomain of a PPCA or a pPPCA.

A biological activity of PPCA or pPPCA can be screened according to known screening assays. The minimum peptide sequence to have activity is based on the smallest unit containing or comprising a particular domain. subdomain, fragment, region. consensus sequence. or repeating unit thereof, having at least one biological activity of a PPCA or pPPCA. such as protecting activity, inhibiting activity or enzyme activity. Non-limiting examples of such activities are: protecting activity for β-galactosidase or neuraminidase (NA); modulating activity (inhibition, stimulation or activation) as an for endothelin I (serine carboxypeptidase) or cathepsin A and peptide hydrolyzing activity (*e.g..* substance P and substance P-free acid; oxytocin and oxytocin-free acid; neurokinin A; angiotensin I; and bradykinin.

According to the present invention. a PPCA or pPPCA includes an association of two or more polypeptide subdomains, such as at least one 4 amino acid portion of a core or cap domain of a PPCA or pPPCA. This can include 1-14 subdomains of the cap domain and/or 1-44 subdomains of the core domain (as monomers or dimers). or any range, value or combination thereof. Preferably 1-4 sets of each of at least one core or cap domains or subdomains are included.

The structure of a monomer or domain of at least one PPCA includes at least one subdomain of a PPCA of a pPPCA of the present invention can include one or more of the following subdomains, as described herein. Generally a PPCA or pPPCA consists of a dimer of a core domain and a cap domain having the following subdomains having the specified residues. e.g.. as presented in Figure 13 (pPPCA) or Figure 14 (PPCA)::

Core domain subdomains: Cβ1, 21-27; Cβ2, 32-39; Cβ3, 50-54; Cα1, 63-67; Cβ4, 73-75; Cβ5, 82-84; Cβ6, 94-98; Cα2, 118-135; Cβ7, 144-149; Cα3, 152-163; Cβ8, 171-177; Cα4, 307-313; Cα5, 316-321; Cα6, 336-341; Cα7, 350-359; Cβ9, 363-369; Cα8, 377-386; Cβ10, 391-401; Cβ11, 407-416; Cβ12, 419-424; Cα9, 431-434; Cα10, 436-447; and

Cap domain subdomains: Hα1, 183-196; Hα2, 202-212; Hα 3, 226-240; Mβ1, 261-264; Mβ2, 267-270; Mα1, 290-293; Mβ3, 296-299. Note that for monomer 2 the secondary structure assignments in the cap domain are slightly different than in monomer 1.

A PPCA or pPPCA polypeptide of the invention can have at least 80% homology, such as 80-100% overall homology or identity, with one or more corresponding PPCA or pPPCA subdomains or fragments as described herein, such as a 4-542 amino acid fragment or portion of the amino acid sequence of Figures 13, 14 or 15. As would be understood by one of ordinary skill in the art, the above configurations of subdomains are provided as part of a PPCA or pPPCA polypeptide of the invention, when expressed in a suitable host cell, or otherwise synthesized, to provide at least one structural or functional feature of a native PPCA or pPPCA, such as at least one PPCA-related biological activity. Such activities can be assayed using a suitable assay, to establish at least one PPCA biological activity of one or more PPCAs or pPPCAs of the invention. A PPCA or pPPCA polypeptide of the invention is not naturally occurring or is naturally occurring but is in a purified or isolated form which does not occur in nature. Examples of suitable PPCA activity assay include, e.g., cathepsin A activity (Galjart et al., J. Biol. Chem. 266:14754-14762 (1991); Endothelin I deamidase activity (Jackman, et al., J. Biol. Chem. 267:2872-2875(1992); and tachykinin deamidase activity (Jackman,. et al., J. Biol. Chem. 265:11265-11272 (1990)).

Percent homology or identity can be determined, for example, by comparing sequence information using the GAP computer program, version 6.0, available from the University of Wisconsin Genetics Computer Group (UWGCG). The GAP program utilizes the alignment method of Needleman and Wunsch (J. Mol. Biol. 48:443 (1970), as revised by Smith and Waterman (Adv. Appl. Math. 2:482 (1981). Briefly, the GAP program defines similarity as the number of aligned symbols (i.e., nucleotides or amino acids) which are similar, divided by the total number of symbols in the shorter of the two sequences. The preferred default parameters for the GAP program include: (1) a unitary comparison matrix (containing a value of 1 for identities and 0 for non-identities) and the weighted comparison matrix of Gribskov and Burgess, Nucl. Acids Res. 14:6745 (1986), as described by Schwartz and Dayhoff, eds., ATLAS OF PROTEIN SEQUENCE AND STRUCTURE, National Biomedical Research Foundation, pp. 353-358 (1979); (2) a penalty of 3.0 for each gap and an additional 0.10 penalty for each symbol in each gap; and (3) no penalty for end gaps.

Thus, one of ordinary skill in the art, given the teachings and guidance presented in the present specification, will know how to add, delete or substitute other amino acid residues in other positions of a PPCA or pPPCA to obtain substituted, deletional or additional variants thereof.

Non-limiting examples of substitutions of a PPCA or pPPCA domains or polypeptide of the invention are those in which at least one amino acid residue in the protein molecule has been removed and a different residue added in its place according to the following Table 2. The types of substitutions which can be made in the protein or peptide molecule of the invention can be based on analysis of the frequencies of amino acid changes between a homologous protein of different species, such those presented in Figure 15. Based on such an analysis, alternative substitutions are defined herein as exchanges within one of the following five groups:

1   Small aliphatic, nonpolar or slightly polar residues: Ala. Ser. Thr (Pro. Gly):
2.   Polar, negatively charged residues and their amides: Asp. Asn. Glu. Gln:
3.   Polar, positively charged residues:
        His. Arg. Lys:
4.   Large aliphatic, nonpolar residues:
        Met. Leu. Ile. Val (Cys); and
5.   Large aromatic residues: Phe. Tyr. Trp.

Most deletions and additions, and substitutions according to the invention are those which do not produce radical changes in the characteristics of the protein or peptide molecule. "Characteristics" is defined in a non-inclusive

manner to define both changes in secondary structure, e.g. α-helix or β-sheet, as well as changes in physiological activity, e.g., in biological activity assays. However, when the exact effect of the substitution, deletion, or addition is to be confirmed, one skilled in the art will appreciate that the effect of at least one substitution, addition or deletion will be evaluated by at least one PPCA or pPPCA screening assay, such as, but not limited to, immunoassays or bioassays, to confirm at least one PPCA or pPPCA biological activity.

Surprisingly, a PPCA and/or a pPPCA is now discovered to have serine carboxypeptidase activity and corresponding structural features, although having only about 30% sequence identity to wheat and yeast serine carboxypeptidases. These carboxypeptidases are members of the hydrolase fold family (Liao *et al.*, *Biochemistry 31*:9796-9812 (1992); Endrizzi *et al.*,*Biochemistry 33*:11106-11120 (1994); Ollis *et al.*, *Protein Eng. 5*:197-211 (1992)). The serine carboxypeptidases have peptidase activity at acidic pH (pH 4.5-5.5) as well as deamidase and esterase activities at pH 7 (reviewed in Breddam *et al. Carlsberg Res. Commun. 51*:83-128 (1986); Rawlings & Barrett, *Methods in Enzymology. 244*:19-61 (1994)). Mutagenesis studies and enzymatic assays have revealed that only the mature form of PPCA possesses a serine carboxypeptidase activity, which is similar to that of lysosomal cathepsin A, and has a preference for hydrophobic substrates such as the dipeptide Phe-Ala (Galjart *et al.*, *J. Biol. Chem. 266*:14754-14762 (1991)). On the basis of sequence alignments with members of the serine carboxypeptidase family, mutagenesis studies and the structure determination of pPPCA, the catalytic triad in PPCA has now been determined to be formed by the residues Ser 150, His 429 and Asp 372

PPCA and pPPCA Expression for Isolation and Purification

A nucleic acid sequence encoding a PPCA or a pPPCA (Galjart *et al.*, *Cell. 54*:755-764 (1988)) can be recombined with vector DNA in accordance with conventional techniques, including blunt-ended or staggered-ended termini for ligation, restriction enzyme digestion to provide appropriate termini, filling in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid undesirable joining, and ligation with appropriate ligases. Techniques for such manipulations are disclosed, *e.g.*, in Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, Second edition, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1989); and Ausubel *et al.*,*Current Protocols in Molecular Biology*, Wiley Interscience, N.Y., (1988-1995) and are well known in the art.

A nucleic acid molecule, such as DNA, is said to be "capable of expressing" a polypeptide if it contains nucleotide sequences which contain transcriptional and translational regulatory information and such sequences are "operably linked" to nucleotide sequences which encode the polypeptide. An operable linkage is a linkage in which the regulatory DNA sequences and the DNA sequence sought to be expressed are connected in such a way as to permit gene expression as a PPCA , pPPCA or fragment thereof, in recoverable amounts. The precise nature of the regulatory regions needed for gene expression can vary from organism to organism, as is well known in the analogous art. See, *e.g.*, Sambrook, *infra* and Ausubel, *infra*.

The invention accordingly encompasses the expression of a PPCA or a pPPCA, in either prokaryotic or eukaryotic cells, although eukaryotic expression is preferred. Preferred hosts are bacterial or eukaryotic hosts including bacteria, yeast, insects, fungi, bird and mammalian cells either *in vivo*, or *in situ*, or host cells of mammalian, insect, bird or yeast origin. It is preferred that the mammalian cell or tissue is of human, primate, hamster, rabbit, rodent, cow, pig, sheep, horse, goat, dog or cat origin, but any other mammalian cell can be used.

Eukaryotic hosts can include yeast, insects, fungi, and mammalian cells either *in vivo*, or in tissue culture. Preferred eukaryotic hosts can also include, but are not limited to insect cells, mammalian cells either *in vivo*, or in tissue culture. Preferred mammalian cells include *Xenopus* oocytes, HeLa cells, cells of fibroblast origin such as VERO or CHO-K1, or cells of lymphoid origin and their derivatives.

Mammalian cells provide post-translational modifications to protein molecules including correct folding or glycosylation at correct sites. Mammalian cells which can be useful as hosts include cells of fibroblast origin such as, but not limited to. NIH 3T3, VERO or CHO, or cells of lymphoid origin, such as, but not limited to, the hybridoma SP2/O-Ag14 or the murine myeloma P3-X63Ag8. hamster cell lines (e.g., CHO-K1 and progenitors, e.g., CHO-

DUXB11) and their derivatives. One preferred type of mammalian cells are cells which are intended to replace the function of the genetically deficient cells *in vivo*. Neuronally derived cells are preferred for gene therapy of disorders of the nervous system.   For a mammalian cell host, many possible vector systems are available for the expression of at least one PPCA or pPPCA. A wide variety of transcriptional and translational regulatory sequences can be employed,

5   depending upon the nature of the host. The transcriptional and translational regulatory signals can be derived from viral sources, such as, but not limited to, adenovirus, bovine papilloma virus, Simian virus, or the like, where the regulatory signals are associated with a particular gene which has a high level of expression. Alternatively, promoters from mammalian expression products, such as, but not limited to, actin, collagen, myosin, protein production.

When live insects are to be used, silk moth caterpillars and baculoviral vectors are presently preferred hosts

10   for large scale PPCA or pPPCA production according to the invention. Production of PPCA or pPPCA in insects can be achieved, for example, by infecting the insect host with a baculovirus engineered to express transmembrane polypeptide by methods known to those skilled in the related arts. See Ausubel *infra*, §§16.8-16.11.

In a preferred embodiment, the introduced nucleotide sequence will be incorporated into a plasmid or viral vector capable of autonomous replication in the recipient host. Any of a wide variety of vectors can be employed for

15   this purpose. See, *e.g.*, Ausubel *et al.*, *infra*, §§ 1.5, 1.10, 7.1, 7.3, 8.1, 9.6, 9.7, 13.4, 16.2, 16.6, and 16.8-16.11. Factors of importance in selecting a particular plasmid or viral vector include: the ease with which recipient cells that contain the vector can be recognized and selected from those recipient cells which do not contain the vector: the number of copies of the vector which are desired in a particular host; and whether it is desirable to be able to "shuttle" the vector between host cells of different species.

20   Different host cells have characteristic and specific mechanisms for the translational and post-translational processing and modification (*e.g.*, glycosylation, cleavage) of proteins. Appropriate cell lines or host systems can be chosen to ensure the desired modification and processing of the foreign protein expressed. For example, expression in a bacterial system can be used to produce an unglycosylated core protein product. Expression in yeast will produce a glycosylated product. Expression in mammalian cells can be used to ensure "native" glycosylation of the heterologous

25   PPCA or pPPCA. Furthermore, different vector/host expression systems can effect processing reactions such as proteolytic cleavages to different extents.

As discussed above, expression of PPCA or pPPCA in eukaryotic hosts requires the use of eukaryotic regulatory regions. Such regions will, in general, include a promoter region sufficient to direct the initiation of RNA synthesis. *See, e.g.*, Ausubel, *infra*; Sambrook, *infra*.

30   Once the vector or nucleic acid molecule containing the construct(s) has been prepared for expression, the DNA construct(s) can be introduced into an appropriate host cell by any of a variety of suitable means, i.e., transformation, transfection, conjugation, protoplast fusion, electroporation, particle gun technology, calcium phosphate-precipitation, direct microinjection, and the like. After the introduction of the vector, recipient cells are grown in a selective medium, which selects for the growth of vector-containing cells. Expression of the cloned gene molecule(s) results in the

35   production of a PPCA or pPPCA. This can take place in the transformed cells as such, or following the induction of these cells to differentiate (for example, by administration of bromodeoxyuracil to neuroblastoma cells or the like).

A PPCA or pPPCA, or fragments thereof, of this invention can be obtained by expression from recombinant DNA according to known methods. Alternatively, a PPCA or pPPCA can be purified from biological material. A PPCA or a pPPCA can be purified from different mammalian tissues (*e.g.*, human placenta, rat liver, mouse liver, pig kidney,

40   bovine testes, bovine liver, and the like) of various genus and species.

The PPCA or pPPCA can be isolated and purified in accordance with conventional method steps, such as extraction, precipitation, chromatography, affinity chromatography, electrophoresis, or the like. For example, cells expressing at least one PPCA or pPPCA in suitable levels can be collected by centrifugation, or with suitable buffers, lysed, and the protein isolated by column chromatography, for example, on DEAE-cellulose, phosphocellulose,

45   polyribocytidylic acid-agarose, hydroxyapatite or by electrophoresis or immunoprecipitation. Alternatively, a pPPCA

or PPCA can be isolated by the use of antibodies. such as. but not limited to. a PPCA- or pPPCA-specific antibody. Such antibodies can be obtained by known method steps (see. e.g.. Harlow and Lane *ANTIBODIES: A LABORATORY MANUAL* Cold Spring Harbor Laboratory (1988); Colligan *et al.*, eds.. *Current Protocols in Immunology*, Greene Publishing Assoc. and Wiley Interscience, N.Y., (1992, 1993). the contents of which references are entirely incorporated

5   herein by reference).

A PPCA or a pPPCA can be purified from different mammalian tissues (e.g.. human placenta, rat liver, mouse liver, pig kidney, bovine testes. bovine liver, and the like) of various genus and species, using known techniques such as gel filtration, phase separation and affinity chromatography, e.g..using polyclonal or monoclonal antibodies specific for a PPCA or pPPCA, according to known methods. *See.. e.g..* Oxender *et al.. Protein Engineering.* Liss, New York

10   (1986).

Overview of PPCA or pPPCA Purification and Crystallization Methods

In general. a PPCA or pPPCA is isolated in soluble form in sufficient purity and concentration (e.g.. a monomer or dimer) for crystallization. The PPCA or pPPCA is then isolated and assayed for biological activity (e.g.. cathepsin A) and for lack of aggregation (which interferes with crystallization). The purified PPCA or pPPCA preferably runs

15   as a single band for each monomer under reducing or nonreducing polyacrylamide gel electrophoresis (PAGE) (nonreducing is used to evaluate the presence of cysteine bridges).

The purified PPCA or pPPCA is preferably crystallized under varying conditions of at least one of the following: pH. buffer type, buffer concentration, salt type, polymer type, polymer concentration. other precipitating ligands and concentration of purified PPCA or pPPCA. See. *e.g..* known methods (Blundell *et al.. Protein*

20   *Crystallography.* Academic Press, London (1976); Oxender. *infra*; McPherson, *The Preparation and Analysis of Protein Crystals,* Wiley Interscience, N.Y. (1982)) or methods provided in a commercial kit, such as CRYSTAL SCREEN (Hampton Research. Riverside, CA). The crystallized PPCA protein can optionally be tested for at least one PPCA activity and differently sized and shaped crystals are further tested for suitability for x-ray diffraction. Generally, larger crystals provide better crystallographic data than smaller crystals. and thicker crystals provide better crystallographic

25   data than thinner crystals. *See. e.g..* Blundell, *infra*; Oxender, *infra*; McPherson, *infra*; Wyckoff *et al.. Diffraction Methods for Biological Macromolecules* Vols. 114-115, *Methods in Enzymology,* Academic Press. Orlando, FL (1985).
Protein Crystallization Methods

The hanging drop method is preferably used to crystallize the purified protein. *See. e.g.,* Blundell, *infra*; Oxender, *infra*; McPherson, *infra*; Wyckoff, *infra*; Taylor *et al.. J. Mol. Biol. 226*:1287-1290 (1992); Takimoto *et al.*

30   (1992). *infra*; CRYSTAL SCREEN. Hampton Research.

A mixture of the purified protein and precipitant can include the following:
- pH (e.g.. 7-9);
- buffer type (e.g.. tromethamine (TRIZMA), sodium azide (NaN$_3$), phosphate, sodium, or cacodylate acetates. imidazole, Tris HCl, sodium hepes);

35   - buffer concentration (e.g., 1-100 mM);
- salt type (e.g.. sodium azide. calcium chloride. sodium citrate. magnesium chloride. ammonium acetate, ammonium sulfate, potassium phosphate. magnesium acetate, zinc acetate: calcium acetate)
- polymer type and concentration: (e.g.. polyethylene glycol (PEG) 1-50%, type 400-10.000);
- other additives (salts: potassium. sodium. tartrate. ammonium sulfate. sodium acetate. lithium sulfate.

40   sodium formate. sodium citrate, magnesium formate. sodium phosphate. potassium phosphate: organics: 2-propanol: non-volatile: 2-methyl-2,4-pentanediol); β-octyl glucoside and
- concentration of purified PPCA or pPPCA (e.g.. 1.0-100 mg/ml).

See. e.g.. CRYSTAL SCREEN. Hampton Research.

A non-limiting example of such crystallization conditions is the following:

45   - purified PPCA or pPPCA protein (e.g.. 5 mg/ml);

• (2) solutions in serial mixtures

(1) 40-80 mM TRIZMA, 0.05-2.0 mM NaN₃,;

(2) 2-30% Polyethylene glycol (PEG) 8000 buffered with 40-80 mM TRIZMA and 0.05-2.0 mM NaN₃,

• 0.05-0.5% β-octyl glucoside;

• at an overall pH of about 8.0-8.3.

The above mixtures are used and screened by varying at least one of pH, buffer type, buffer concentration, precipitating salt type or additive or their concentrations, PEG type, PEG concentration, and protein concentration. Crystals ranging in size from 0.1-0.9 mm are formed in 1 -14 days. These crystals diffract x-rays to at least 10 Å resolution, such as 0.15-10.0 Å, or any range of value therein, such as 1.5, 1.6, 1.7. 1.8, 1.9, 2.0, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3.0, 3.1, 3.2, 3.3, 3.4 or 3.5, with 3.5 Å or higher being preferred for the highest resolution. In addition to diffraction patterns having this highest resolution, lower resolution, such as 25-3.5 Å can also be used. *See, e.g.,* Blundell, *infra*; Oxender, *infra*; McPherson, *infra*; Wyckoff, *infra*;

Protein Crystals

Crystals appear after 1-14 days and continue to grow on subsequent days. Some of the crystals can be optionally removed, washed, and assayed for biological activity (*e.g.,* PPCA), which activity is preferred for using in further characterizations. Other washed crystals are preferably run on a gel and stained, and those that migrate in the same position as the purified PPCA or pPPCA are preferably used. From two to one hundred crystals are observed in one drop and crystal forms can occur, such as, but not limited to, orthorombic, bipyramidal, rhomboid, and cubic. Initial x-ray analyses indicate that such crystals diffract at moderately high to high resolution. When fewer crystals are produced in a drop, they can be much larger size, *e.g.,* 0.4-0.9 mm. *See, e.g.,* Blundell, *infra*; Oxender, *infra*; McPherson, *infra*; Wyckoff, *infra*;

PPCA and pPPCA X-ray Crystallography Methods

The crystals so produced for a PPCA or pPPCA are x-ray analyzed using a suitable x-ray source. Diffraction patterns are obtained. Crystals are preferably stable for at least 10 hrs in the x-ray beam . Frozen crystals (*e.g.,* -220 to -50°C) are optionally used for longer x-ray exposures (*e.g.,* 5-72 hrs), the crystals being relatively more stable to the x-rays in the frozen state. To collect the maximum number of useful reflections, multiple frames are optionally collected as the crystal is rotated in the x-ray beam, *e.g.,* for 5-72 hrs. Larger crystals (>0.2 mm) are preferred, to increase the resolution of the x-ray diffraction patterns obtained. Crystals are preferably analyzed using a synchrotron high energy x-ray source. Using frozen crystals, x-ray diffraction data is collected on crystals that diffract to at least a relatively high resolution of 10-1.5 Å, with lower resolutions also useful, such as 25-10Å, sufficient to solve the three-dimensional structure of a PPCA or pPPCA in considerable detail, as presented herein.

Passing an x-ray beam through a crystal produces a diffraction pattern as a result of the x-rays interacting and being scattered by the contents of the crystal. The diffraction pattern can be visualized using, *e.g.,* an image plate or film, resulting in an image with spots corresponding to the diffracted x-rays. The positions of the spots in the diffraction pattern are used to determine parameters intrinsic to the crystal (such as unicell parameters) and to gain information on the packing of the molecules in the crystal. The intensity of the spots contains the Fourier transformation of the molecules in the crystal, *i.e.,* information on each atom in the crystal and hence of the crystallized molecule.

After data collection of diffraction patterns, the data is processed. This includes measuring the spots on each diffraction pattern in terms of position and intensity. This information is processed (*i.e.,* mathematical operations are performed on the data (such as scaling, merging and converting the data from intensity of diffracted beams to amplitudes)) to yield a set of data which is in a form as can be used for the further structure determination of the molecule crystallized. The amplitudes of the diffracted x-rays are then combined with calculated phases to produce an electron density map of the contents of the crystal. In this electron density map, the structure of the molecules (as

present in the crystal) is built. The phases can be determined with various known techniques, one being molecular replacement.

For the molecular replacement technique one takes a known three dimensional structure thought to share structural homology with the structure to be determined, to generate after calculations a first set of initial phases. These
5   phases are then combined with the diffraction information of the molecule for which you want to solve the structure of. The result is an electron density map of the molecules in the crystal from which the diffraction patterns originate.

The phases can be further optimized using a technique called density modification, which allows electron density maps of better quality to be produced facilitating interpretation and model building therein. The atomic model is then refined by allowing the atoms in the model to move in order to match the diffraction data as well as possible
10   while continuing to satisfy stereochemical constraints (sensible bond lengths, bond angles and the like). *See, e.g.,* Blundell, *infra*; Oxender, *infra*; McPherson, *infra*; Wyckoff, *infra*;

Computer Related Embodiments

An amino acid sequence of a PPCA or pPPCA and/or atomic coordinate/x-ray diffraction data, useful for computer structure determination of a PPCA, pPPCA or a portion thereof, can be "provided" in a variety of mediums
15   to facilitate use thereof. As used herein, provided refers to a manufacture, which contains a PPCA or pPPCA amino acid sequence and/or atomic coordinate/x-ray diffraction data of the present invention, *e.g.*, the amino sequence provided in Figures 13-15, a representative fragment thereof, or an amino acid sequence having at least 80-100% overall identity to a 5-542 amino acid fragment of an amino acid sequence of Figures 13-15. Such a method provides the amino acid sequence and/or atomic coordinate/x-ray diffraction data in a form which allows a skilled artisan to analyze and
20   determine the three- dimensional structure of a PPCA, a pPPCA or a subdomain thereof.

In one application of this embodiment, PPCA, pPPCA, or at least one subdomain thereof, amino acid sequence and/or atomic coordinate/x-ray diffraction data of the present invention is recorded on computer readable media. As used herein, "computer readable media" refers to any medium which can be read and accessed directly by a computer. Such media include, but are not limited to: magnetic storage media, such as floppy discs, hard disc storage medium, and
25   magnetic tape; optical storage media such as optical discs or CD-ROM; electrical storage media such as RAM and ROM; and hybrids of these categories such as magnetic/optical storage media. A skilled artisan can readily appreciate how any of the presently known computer readable media can be used to create a manufacture comprising computer readable medium having recorded thereon an amino acid sequence and/or atomic coordinate/x-ray diffraction data of the present invention.

30   As used herein, "recorded" refers to a process for storing information on computer readable medium. A skilled artisan can readily adopt any of the presently known methods for recording information on computer readable medium to generate manufactures comprising an amino acid sequence and/or atomic coordinate/x-ray diffraction data information of the present invention.

A variety of data storage structures are available to a skilled artisan for creating a computer readable medium
35   having recorded thereon an amino acid sequence and/or atomic coordinate/x-ray diffraction data of the present invention. The choice of the data storage structure will generally be based on the means chosen to access the stored information. In addition, a variety of data processor programs and formats can be used to store the sequence and x-ray data information of the present invention on computer readable medium. The sequence information can be represented in a word processing text file, formatted in commercially-available software such as WordPerfect and MICROSOFT Word,
40   or represented in the form of an ASCII file, stored in a database application, such as DB2, Sybase, Oracle, or the like. A skilled artisan can readily adapt any number of dataprocessor structuring formats (e.g. text file or database) in order to obtain computer readable medium having recorded thereon the information of the present invention.

By providing on computer readable media having stored therein a PPCA or pPPCA sequence and/or atomic coordinates based on x-ray diffraction data, a skilled artisan can routinely access the sequence and atomic coordinate
45   or x-ray diffraction data to model a PPCA, pPPCA, a subdomain thereof, or a ligand thereof. Computer algorithms are

publicly and commercially available which allow a skilled artisan to access this data provided on a computer readable medium and analyze it for structure determination and/or RDD. *See, e.g., Biotechnology Software Directory.* Mary Ann Liebert Publ., New York (1995).

5   The present invention further provides systems, particularly computer-based systems, which contain the sequence and/or diffraction data described herein. Such systems are designed to do structure determination and RDD for a PPCA, pPPCA or at least one subdomain thereof. Non-limiting examples are microcomputer workstations available from Silicon Graphics Incorporated and Sun Microsystems running Unix based. Windows NT or IBM OS/2 operating systems.

10   As used herein, "a computer-based system" refers to the hardware means, software means, and data storage means used to analyze the sequence and/or atomic coordinate/x-ray diffraction data of the present invention. The minimum hardware means of the computer-based systems of the present invention comprises a central processing unit (CPU), input means. output means, and data storage means. A skilled artisan can readily appreciate which of the currently available computer-based system are suitable for use in the present invention. A monitor is optionally provided to visualize structure data.

15   As stated above, the computer-based systems of the present invention comprise a data storage means having stored therein a PPCA, pPPCA or fragment sequence and/or atomic coordinate/x-ray diffraction data of the present invention and the necessary hardware means and software means for supporting and implementing an analysis means. As used herein. "data storage means" refers to memory which can store sequence or atomic coordinate/x-ray diffraction data of the present invention, or a memory access means which can access manufactures having recorded thereon the

20   sequence or x-ray data of the present invention.

As used herein, "search means" or "analysis means" refers to one or more programs which are implemented on the computer-based system to compare a target sequence or target structural motif with the sequence or x-ray data stored within the data storage means. Search means are used to identify fragments or regions of a PPCA or pPPCA which match a particular target sequence or target motif. A variety of known algorithms are disclosed publicly and a

25   variety of commercially available software for conducting search means are and can be used in the computer-based systems of the present invention. A skilled artisan can readily recognize that any one of the available algorithms or implementing software packages for conducting computer analyses that can be adapted for use in the present computer-based systems.

As used herein, "a target structural motif," or "target motif," refers to any rationally selected sequence or

30   combination of sequences in which the sequence(s) are chosen based on a three-dimensional configuration or electron density map which is formed upon the folding of the target motif. There are a variety of target motifs known in the art. Protein target motifs include, but are not limited to, enzymic active sites, structural subdomains, epitopes, functional domains and signal sequences. A variety of structural formats for the input and output means can be used to input and output the information in the computer-based systems of the present invention.

35   A variety of comparing means can be used to compare a target sequence or target motif with the data storage means to identify structural motifs or interpret electron density maps derived in part from the atomic coordinate/x-ray diffraction data. A skilled artisan can readily recognize that any one of the publicly available computer modeling programs can be used as the search means for the computer-based systems of the present invention.

One application of this embodiment is provided in Figure 22. Figure 22 provides a block diagram of a

40   computer system 102 that can be used to implement the present invention. The computer system 102 includes a processor 106 connected to a bus 104. Also connected to the bus 104 are a main memory 108 (preferably implemented as random access memory. RAM) and a variety of secondary storage memory 110. such as a hard drive 112. a removable storage medium 114. and a monitor 120. The removable medium storage device 114 may represent, for example. a floppy disk drive. a CD-ROM drive. a magnetic tape drive. etc. A removable storage medium 116 (such as a floppy

45   disk. a compact disk. a magnetic tape. etc.) containing control logic and/or data recorded therein may be inserted into

the removable medium storage medium 114. The computer system 102 includes appropriate software for reading the control logic and/or the data from the removable medium storage device 114 once inserted in the removable medium storage device 114.

5　　　　Amino acid, encoding nucleotide or other sequence and/or atomic coordinate/x-ray diffraction data of the present invention may be stored in a well known manner in the main memory 108, any of the secondary storage devices 110, and/or a removable storage device 116. Software for accessing and processing the amino acid sequence and/or atomic coordinate/x-ray diffraction data (such as search tools, comparing tools, etc.) reside in main memory 108 during execution. The monitor 120 is optionally used to visualize the structure data.

Structure Determination

10　　　　One or more computational steps, computer programs and/or computer algorithms are used to build a molecular 3-D model of a PPCA or pPPCA, using amino acid sequence data from Figures 13-15 (or variants thereof) and/or atomic coordinate/x-ray diffraction data, as presented herein.

In x-ray crystallography, x-ray diffraction data and phases are combined to produce electron density maps in which the three-dimensional structure of a PPCA or pPPCA is then built or modeled. This structure can then be used

15　for RDD of modulators of at least one PPCA- or pPPCA-related activity that is relevant to at least one PPCA- or pPPCA-related pathology.

Density Modification and Map Interpretation. Electron density maps can be calculated using such programs as those from the CCP4 computing package (SERC (UK) Collaborative Computing Project 4, Daresbury Laboratory, UK, 1979). Cycles of two-fold averaging can further be used, such as with the program RAVE (Kleywegt & Jones,

20　Bailey *et al.*, eds., *First Map to Final Model*, SERC Daresbury Laboratory, UK, pp 59-66 (1994)) and gradual model expansion. For map visualization and model building a program such as "O" (Jones (1991), *infra*) can be used.

Refinement and Model Validation. Rigid body and positional refinement can be carried out using a program such as X-PLOR (Brünger (1992), *infra*), e.g., with the stereochemical parameters of Engh and Huber (*Acta Cryst. A47*:392-400 (1991)). If the model at this stage in the averaged maps still misses residues (e.g., at least 5-10 per

25　subunit), the some or all of the missing residues can be incorporated in the model during additional cycles of positional refinement and model building. The refinement procedure can start using data from lower resolution (e.g., 25-10Å to 10-3.0 Å and then gradually extended to include data from 12-6Å to 3.0-1.5 Å. B-values (also termed temperature factors) for individual atoms can be refined once data of 2.8Å or higher (e.g., up to 1.5 Å) has been added. Subsequently waters can be gradually added. A program such as ARP (Lamzin and Wilson, *Acta Cryst. D49*:129-147 (1993)) can be

30　used to add crystallographic waters and as a tool to check for bad areas in the model. Programs such as PROCHECK (Lackowski *et al.*, *J. Appl. Cryst. 26*:283-291 (1993)), WHATIF (Vriend, *J. Mol. Graph. 8*:52-56 (1990)) and PROFILE 3D (Lüthy *et al.*, *Nature 356*:83-85 (1992)), as well as the geometrical analysis generated by X-PLOR can be been used to check the structure for errors. A program such as DSSP can be used to assign the secondary structure elements (Kabsch and Sander (1983), *infra*).

35　　　　The structure of a PPCA or pPPCA can thus be solved with the molecular replacement procedure such as by using X-PLOR (Brünger (1992), *infra*). A partial search model for the monomer can be constructed using a related protein, such as wheat serine carboxypeptidase structure (Liao *et al.* (1992), *infra*). The rotation and translation function can be solved to yield orientations and positions for the subunits in the crystallographic asymmetric unit. This allows phases to be determined that, when combined with information from the x-ray diffraction patterns, allows electron

40　density maps of a PPCA or pPPCA to be calculated. The atomic model is then built using these electron density maps. Cyclical two-fold density averaging can also be done to improve the electron density maps using a suitable program (e.g., RAVE) and model expansion can also be used to add missing residues for each monomer, resulting in a model with 95-99.9% of the total number residues. The model can be refined in a program such as X-PLOR (Brünger (1992), *supra*), to a suitable crystallographic R$_{factor}$. The model data is then saved on computer readable media for use in further

45　analysis, such as rational drug design.

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Rational Design of Drugs that Interact with the PPCA or pPPCA

The determination of the three-dimensional structure of a PPCA or pPPCA, as described herein, provides a basis for the design of new and specific ligands for the diagnosis and/or treatment of at least one PPCA- or pPPCA-related pathology.

5   Several approaches can be taken for the use of the crystal structure of a PPCA or pPPCA in the rational design of ligands of this protein. A computer-assisted, manual examination of the active site structure is optionally done. The use of software such as GRID (Goodford, *J. Med. Chem.* 28:849-857 (1985)) a program that determines probable interaction sites between probes with various functional group characteristics and the enzyme surface — is used to analyze the active site to determine structures of inhibiting compounds. The program calculations, with suitable

10   inhibiting groups on molecules (*e.g.*, protonated primary amines) as the probe, are used to identify potential hotspots around accessible positions at suitable energy contour levels. Suitable ligands, as inhibiting or stimulating modulating compounds or compositions. are then tested for modulating activities of at least one PPCA or pPPCA .

A diagnostic or therapeutic PPCA or pPPCA modulating ligand of the present invention can be, but is not limited to, at least one selected from a nucleic acid, a compound, a protein, an element, a lipid, an antibody, a saccharide,

15   an isotope, a carbohydrate, an imaging agent, a lipoprotein, a glycoprotein, an enzyme, a detectable probe, and antibody or fragment thereof. or any combination thereof, which can be detectably labeled as for labeling antibodies. Such labels include, but are not limited to. enzymatic labels, radioisotope or radioactive compounds or elements, fluorescent compounds or metals, chemiluminescent compounds and bioluminescent compounds. Alternatively, any other known diagnostic or therapeutic agent can be used in a method of the invention.

20   After preliminary experiments are done to determine the K_m of the substrate with each enzyme activity of a PPCA or pPPCA. the time-dependent nature of modulation of ligand K, values are determined, (*e.g.*, by the method of Henderson (*Biochem. J.* 127:321-333 (1972)). For example, the substrate (or blank where appropriate) and enzyme are pre-incubated in buffer. Reactions are initiated by the addition of substrate. Aliquots are removed over a suitable time course and each quenched by addition into the aliquots of suitable quenching solution (*e.g.*, sodium hydroxide in

25   aqueous ethanol). The concentration of product is determined, *e.g.*, fluorometrically, using a spectrometer . Plots of fluorescence against time can be close to linear over the assay period, and are used to obtain values for the initial velocity in the presence (V_i) or absence (V_o) of ligand. Error is present in both axes in a Henderson plot, making it inappropriate for standard regression analysis (Leatherbarrow, *Trends Biochem. Sci.* 15:455-458 (1990)). Therefore, K_i values are obtained from the data by fitting to a modified version of the Henderson equation for competitive inhibition:

30

$$Qr^2 + (E_t - Q - I)r - E_t = 0$$

where (using the notation of Henderson (*Biochem. J.* 127:321-333 (1972)):

$$Q = K_i \left(\frac{A_t}{K_a} + K_a \right) \quad \text{and} \quad r = \frac{V_o}{V_i}$$

This equation is solved for the positive root with the constraint that

$$Q = K_i((A_t + K_a) / K_a)$$

35   using PROCNLIN from SAS (SAS Institute Inc.. Cary. North Carolina, USA) which performs nonlinear regression using least-square techniques. The iterative method used is optionally the multivariate secant method, similar to the Gauss-Newton method. except that the derivatives in the Taylor series are estimated from the histogram of iterations rather than supplied analytically. A suitable convergence criterion is optionally used, *e.g.*, where there is a change in loss function of less than 10^{-8}.

Once modulating ligands are found and isolated or synthesized, crystallographic studies of the compounds complexed to a PPCA or pPPCA can be performed. As a non-limiting example, PPCA or pPPCA crystals are soaked for 2 days in 0.01-100 mM ligand and x-ray diffraction data are collected on an area detector and/or an image plate detector (e.g., a Mar image plate detector) using a rotating anode x-ray source. Data are collected to as high a resolution as possible, e.g., an inner limit of diffraction of 1.5-3.5Å. An atomic model of the inhibitor is built into the difference Fourier map ($F_{inhibitor\ complex} - F_{native}$). The model can be refined to adjust the atomic positions to improve the fit with the electron density maps, while maintaining correct stereochemical constraints. The model will preferably have low r.m.s. deviations from the ideal bond lengths, as well as for the angles, respectively, as well as a low R-factor (preferably less than about 25-35%, such as less than about 35, 34, 33, 32, 31, 30, 29, 28, 27, 26, or 25%.

Direct measurements of enzyme inhibition provide further confirmation that the modeled ligands are modulators of at least one biological activity of a PPCA or a pPPCA . As a non-limiting example, a modification (Chong et al., Biochim. Biophys. Acta 1077:65-71 (1991)) of the fluorometric assay of Potier (et al., Analyt. Biochem. 94:287-296 (1979)) is optionally used to measure neuraminidase inhibition or stimulation, optionally including determination of inhibition constants (K_i). Other suitable PPCA activity assay include, e.g., cathepsin A activity (Galjart et al., J. Biol. Chem. 266:14754-14762 (1991); Endothelin I deamidase activity (Jackman, et al., J. Biol. Chem. 267:2872-2875(1992); and tachykinin deamidase activity (Jackman, et al., J. Biol. Chem. 265:11265-11272 (1990)).

Ligands of a PPCA or pPPCA, based on the crystal structure of this enzyme, are thus also provided by the present invention. A PPCA or pPPCA ligand is any molecule, compound or composition that is capable of associating with a PPCA or pPPCA and optionally modulating at least one function or structural feature of a PPCA or pPPCA. Preferably, a PPCA or pPPCA ligand modulates at least one biological activity of a PPCA or pPPCA. Demonstration of clinically useful levels, e.g., in vivo activity is also important. In evaluating PPCA or pPPCA inhibitors for biological activity in animal models (e.g., rat, mouse, rabbit) using various oral and parenteral routes of administration are evaluated. Using this approach, it is expected that modulation of a PPCA or pPPCA occurs in suitable animal models, using the ligands discovered by structure determination and x-ray crystallography.

Evaluation of Therapeutic Potentials of Compositions via a PPCA Animal Model

The present invention also provides methods for identifying diagnostic or therapeutic ligands of PPCA or pPPCA via computer RDD, to treat a PPCA-related pathology. Generally, a method for determining the therapeutic or diagnostic use of a PPCA or pPPCA modulating ligand, to treat a PPCA related pathology, comprises the steps of administering a known dose of at least one ligand containing compositions to an animal model having a phenotype corresponding to a PPCA-related pathology, monitoring the appropriate biological or biochemical parameters, and comparing the results with treated animals to those of untreated animals. Results indicating the onset or presence of a PPCA related pathology are generally referred to herein as "symptoms" of the disease. See., e.g., U.S. Appl. No. 08/397,693, filed March 2, 1995, which is entirely incorporated herein by reference.

Appropriate biological and biochemical parameters that reflect the onset and progression of a PPCA related pathology include. but are not limited to, (1) gross biological parameters, e.g., physical appearance (i.e., flattening of the face, rough haircoat and/or subcutaneous swelling in affected animals) or growth (reduced weight gain); (2) gross behavioral parameters, e.g., lack of coordination; (3) biochemical assays, e.g., assays of cathepsin A, N-acetyl-α-neuraminidase or β-galactosidase activities in primary cultures of skin fibroblasts or tissue homogenates; (4) histopathological studies (visceromegaly, i.e., enlarged liver and spleen: accumulation of secondary vacuoles in kidney tissues: etc.).

A first method of evaluating the therapeutic potential of a composition using the transgenic non-human animals of the invention comprises the steps of:

(1)   Administering a known dose of the composition to a first non-human animal having a phenotype corresponding to a human PPCA related pathology;

(2)   Detecting the time of onset of symptoms in the first non-human animal: and

      (3)   Comparing the time of onset of symptoms in the first non-human animal to the time of onset of symptoms in a second non-human animal having a phenotype corresponding to a human PPCA related pathology, which has not been exposed to the composition;

wherein a statistically significant delay in the time of onset of symptoms in the first non-human animal relative to the time of onset of the symptoms in the second non-human animal indicates the potential of the composition for treating a PPCA related pathology.

A second method of evaluating the therapeutic potential of a composition using the non-human animals of the invention comprises the steps of:

      (1)   Administering a known dose of the composition to a first non-human animal having a phenotype corresponding to a human PPCA related pathology at an initial time, t_0;

      (2)   Determining the extent of symptoms in the first non-human animal at a later time, t_1; and

      (3)   Comparing, at t_1, the extent of symptoms in the first non-human animal to the extent of symptoms in a second non-human animal having a phenotype corresponding to a human PPCA related pathology, which has not been exposed to the composition at t_0,

wherein a statistically significant decrease in the extent of symptoms at t_1 in the first non-human animal relative to the extent of the symptoms at t_1 in the second non-human animal indicates the potential of the composition for treating a PPCA related pathology.

In the above methods, the composition being tested may comprise a chemical compound administered by circulatory injection or oral ingestion. The composition being evaluated may alternatively comprise a polypeptide administered by circulatory injection of an isolated or recombinant bacterium or virus that is live or attenuated, wherein the polypeptide is present on the surface of the bacterium or virus prior to injection, or a polypeptide administered by circulatory injection of an isolated or recombinant bacterium or virus capable of reproduction within a non-human animal, and the polypeptide is produced within a non-human animal by genetic expression of a DNA sequence encoding the polypeptide. Alternatively, the composition being evaluated may comprise one or more nucleic acids, including a gene from the human genome or a processed RNA transcript thereof. Similarly, the composition being evaluated may comprise cells removed from a mammal and genetically engineered to overexpress a lysosomal protein or some other therapeutic polypeptide.

Once the PPCA modulating ligand has been shown to be effective in an animal model, it can then be tested in human clinical trials, according to known method steps.

In the above methods, delivery of the composition being tested to non-human animals is achieved via means appropriate for the composition being tested, e.g., by diet; by intermittent or continuous intravenous injection of one or more of the compositions or of a liposome (Rahman and Schein, in *Liposomes as Drug Carriers*, Gregoriadis, ed., John Wiley, New York (1988), pages 381-400; Gabizon, A., in *Drug Carrier Systems*, Vol. 9, Roerdink *et al.*, eds., John Wiley, New York (1989), pages 185-212) or microparticle (Tice *et al.*, U.S. Patent 4,542,025 (Sep. 17, 1985)) formulation comprising one or more of the compositions; via subdermal implantation of drug-polymer conjugates (Duncan, R., *Anti-Cancer Drugs* 3:175-210 (1992); via microparticle bombardment (Sanford *et al.*, U.S. Patent 4,945,050 (Jul. 31, 1990)); via infusion pumps (Blackshear and Rohde, in *Drug Carrier Systems*, Vol. 9, Roerdink *et al.*, eds., John Wiley, New York (1989), pages 293-310) or by other appropriate means known in the art (see, generally, *Remington's Pharmaceutical Sciences*, 18th Ed., Gennaro, ed., Mack Publishing Co., Easton, PA (1990)).

Pharmaceutical/Diagnostic Administration

Using compounds or compositions comprising at least one PPCA or PPCA modulating ligand, the present invention further provides a method for modulating the activity of a PPCA or pPPCA protein in a cell. In general, ligands (antagonists or agonists) which have been identified to inhibit or enhance the activity of at least one PPCA or pPPCA ligand can be formulated so that the ligand can be contacted with a cell expressing at least one PPCA or pPPCA

protein *in vivo*. The contacting of such a cell with such a ligand results in the *in vivo* modulation of at least one biological activity of a PPCA or pPPCA.

At least one PPCA or pPPCA modulating compound or composition of the invention can be administered by any means that achieve the intended purpose, using a suitable pharmaceutical composition or formulation. For example, administration can be by various parenteral routes such as subcutaneous, intravenous, intradermal, intramuscular, intraperitoneal, intranasal, intracranial, transdermal, or buccal routes. Alternatively, or concurrently, administration can be by the oral route. Parenteral administration can be by bolus injection or by gradual perfusion over time.

A typical regimen for treatment or prophylaxis comprises administration of an effective amount over a period of one or several days, up to and including between one week and about six months. It is understood that the dosage of a diagnostic/pharmaceutical compound or composition of the invention administered *in vivo* or *in vitro* will be dependent upon the age, sex, health, and weight of the recipient, kind of concurrent treatment, if any, frequency of treatment, and the nature of the diagnostic/ pharmaceutical effect desired. The ranges of effective doses provided herein are not intended to be limiting and represent preferred dose ranges. However, the most preferred dosage will be tailored to the individual subject, as is understood and determinable by one skilled in the relevant arts. See, *e.g.*, Berkow *et al.*, eds., *The Merck Manual*, 16th edition, Merck and Co., Rahway, N.J., 1992; Goodman *et al.*, eds., *Goodman and Gilman's The Pharmacological Basis of Therapeutics*, 8th edition, Pergamon Press, Inc., Elmsford, N.Y., (1990); *Avery's Drug Treatment: Principles and Practice of Clinical Pharmacology and Therapeutics*, 3rd edition, ADIS Press, LTD., Williams and Wilkins, Baltimore, MD. (1987). Ebadi, *Pharmacology*, Little, Brown and Co., Boston, (1985); Osol *et al.*, eds., *Remington's Pharmaceutical Sciences*, 18th edition, Mack Publishing Co., Easton, PA (1990); Katzung, *Basic and Clinical Pharmacology*, Appleton and Lange, Norwalk, CT (1992), which references are entirely incorporated herein by reference.

The total dose required for each treatment can be administered by multiple doses or in a single dose. The diagnostic/pharmaceutical compound or composition can be administered alone or in conjunction with other diagnostics and/or pharmaceuticals directed to the pathology, or directed to other symptoms of the pathology. Effective amounts of a diagnostic/pharmaceutical compound or composition of the invention are from about 0.1 μg to about 100 mg/kg body weight, administered at intervals of 4-72 hours, for a period of 2 hours to 1 year, and/or any range or value therein.

The recipients of administration of compounds and/or compositions of the invention can be any mammals. Among mammals, the preferred recipients are mammals of the Orders Primata (including humans, apes and monkeys), Arteriodactyla (including horses, goats, cows, sheep, pigs), Rodenta (including mice, rats, rabbits, and hamsters), and Carnivora (including cats, and dogs). The most preferred recipients are humans.

Having now generally described the invention, the same will be more readily understood through reference to the following example which is provided by way of illustration, and is not intended to be limiting of the present invention.

Example 1: Preparation, Purification and Crystallization of PPCA or pPPCA from Human Cells

The present invention provides, in one aspect, the determination of the three-dimensional structure of the human protective protein/cathepsin A (PPCA) in the precursor form (pPPCA) by a combination of molecular replacement and twofold density averaging. The structure presented here is the first of an enzyme associated with a human PPCA related pathology, and the third human lysosomal enzyme structure determined. The structure gives us insight into the zymogen activation mechanism of pPPCA, as well as the expected 3-D structure of PPCA and its specific and new enzymatic activities.

PPCA and pPPCA Expression and Purification

Plasmid Constructs. AcMNPV transfer-plasmids pJR2 and pBC3 (Figure 1) were derivatives of plasmid pAc373, carrying the entire polyhedrin gene (Smith *et al.*, 1985). In pJR2 a polylinker with a number of multiple cloning sites (MCS) was inserted directly 3' of the polyhedrin promoter, and substituted a 33-nucleotide deletion of the

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polyhedrin gene, starting with the ATG. pBC3 had the polylinker situated in a similar position as pJR2, but instead of the 33-nt deletion this plasmid featured an ATG codon mutated in ACG. Full-length human PPCA cDNA, PPCA54 (Galjart et al., 1988), and the two deletion cDNA mutants, 32(Δ20) and 20(Δ32) (Galjart et al., 1991), were subcloned either in pJR2 or pBC3 as EcoRl fragments, using standard procedures (Sambrook et al., 1989). (Figure 1). The
5   20(Δ32) deletion mutant was tagged with the human PPCA signal sequence, as reported earlier (Galjart et al., 1991). All cDNA fragments were engineered to have short 3' and 5' untranslated regions (< 10 bp).

   Transfection and Selection of Recombinant Baculovirus. Spodoptera frugiperda insect cells (IPLB-SF21) were cultured in monolayers at 27°C in TNM-FH medium (Hink, 1970), supplemented with 10% FBS and antibiotics (complete medium). Wild-type (wt) AcMNPV virus strain E2 (Smith and Summers, 1978) and recombinant
10   baculoviruses were propagated on confluent monolayers of Sf21 cells. Recombinant constructs AcPPCA54, AcPPCA32 and AcPPCA20 were generated by cotransfecting Sf21 cells with 1 μg wt-AcMNPV DNA and 10 μg plasmid DNA, using the calcium phosphate method, modified for insect cells (Graham et al., 1973; Carstens et al., 1980; Summers et al., 1987). Recombinant polyhedrin-negative recombinant baculoviruses were then selected and purified by sequential plaque assays, and verified by dot blot and southern blot analysis (Summers et al., 1987). Large quantities of inoculum
15   were produced by infection of insect cells at 25-50 % confluency, with recombinant virus at a multiplicity of infection (MOl) of < 1 pfu/cell. After 3 to 6 days at 27°C, when all cells appeared infected, the medium was harvested and centrifuged for 5 m at 1000 rpm to remove detached cells. The titre of the inoculum was determined by plaque assay analysis.

   Protein purification and western blotting. Sf21 cells were cultured in either 175 CM^2 or 500 CM^2 flasks (triple
20   flask, Nunc) to near confluency, and infected with recombinant baculoviruses at a MOl of 5-10 pfu/cell. After 1.5 h incubation at 27 °C, the inoculum was replaced with complete medium for additional 8 to 10 hrs. Cell monolayers were then rinsed with PBS and cultured further for 38 h in unsupplemented Grace's medium. After infection the medium was collected, centrifuged for 5 m at 1500 g, and for 1 h at 100.000 g (Beckmann SW-28 rotor) to remove virus particles. After centrifugation the supernatant was concentrated 20-fold, in an Amicon stirred cell. Glycoproteins were purified
25   ~60% using a concanavalin A-SEPHAROSE affinity chromatography column, as described earlier (Verheijen et al., 1982). Total protein concentration was measured using the method of Smith et al., (1985). Aliquots of the purified preparation were resolved on 12.5% SDS-polyacrylamide gels under reducing and non-reducing conditions. Gels were either Coomassie brilliant blue- or silver stained (Sambrook et al., 1989). For western blotting, proteins were transferred from gels to IMMOBILON PVDV membranes (Millipore Corp.). using a semidry blotter (The W.E.P. company).

30   *Development and Use of pPPCA antibodies.* A 15 amino acid peptide (NH$_2$-Cys-Met-Trp-His-Gln-Ala-Leu-Leu-Arg-Ser-Glu-Asp-Lys-Ala-Arg-COOH) (Figure 5), based on the C-terminal sequence of the 34-kDa PPCA subunit (amino acid 285-298, Galjart et al., 1988), was synthesized on a peptide synthesizer (Applied Biosystems), and covalently linked to the carrier protein *Keyhole Limpet Hemocvanin*, using the IMJECT ACTIVATED IMMUNOGEN CONJUGATION KIT (Pierce). Polyclonal antibodies against the conjugated product were raised in rabbit, by multiple
35   subdermal injections of the protein (40-125 μg) mixed with incomplete Freunds adjuvant (Pierce). Rabbits were bled 34 days after the first injection. The antibodies, designated anti-pep, were tested on immunoblots and by immunoprecipitations of baculovirus produced PPCA.

   Blots were incubated for at least 12 h in blocking buffer (0.01 M tris-buffered saline pH 8.0 (TBS), 0.05% Tween 20, and 3% (w/v BSA), and subsequently probed for 2 h with polyclonal PPCA antibodies, anti-54, diluted 1:200
40   in fresh blocking buffer. They were then washed for 1 h in TBS. 0.05% Tween 20, and incubated for 2 h with alkaline phosphatase conjugate anti-rabbit IgG (Sigma, 1:1000 in blocking buffer). Proteins were visualized using alkaline phosphatase substrate (Sigma, 4-aminodiphenylamine diazonium sulfate, naphtol as-mx phosphate).

   Crystallization of PPCA. Fractions containing the precursor form of the protein as assayed on an SDS-PAGE gel were pooled. Subsequently the protein was concentrated to 5 mg/ml and the buffer exchanged to 50 mM NaAc pH
45   5.2 or 50 mM MES pH 6.5 using a CENTRICON-1 0. Crystals were grown using the hanging drop vapor diffusion

technique. Crystals suitable for data collection were grown using a reservoir solution containing : 2-10 % PEG 8000, pH 8.0 - 8.3, 50mM TRIZMA, 1mM NaN₃, 0.25 % β-octyl glucoside at 4-12°C. Mixing non-equal volumes of protein solution (in the range 5-10µl) and reservoir solution (in the range 2-6 W) enhanced the occurrence of single large crystals per drop under these crystallization conditions. The concentration of the protein solution before mixing was

5   5 mg/ml. Crystal growth was enhanced by macrocrystallization techniques (anything that promotes growth of big crystals) and in some cases by micro- and macroseeding techniques.

Example 2:   Structure Determination of a pPPCA Crystallized from Human Cells

  Data Collection, Data Processing and Reduction.

       To allow for data collection at cryotemperatures, the crystals were cryoprotected by adding glycerol in 5%-10%
10   steps to a solution of about 12% PEG 8000, 50 mM TRIZMA, pH 8.0, 1mM NaN₃, 0.25% β-octyl glucoside, which served as an artificial mother liquor. The crystals were incubated for half an hour at 40°C after each addition of glycerol. The final mother liquor contained 30% glycerol. Gradually increasing the glycerol was needed to help keep the crystals from cracking.

       Diffraction data was collected at the Stanford Synchrotron Radiation Laboratories (SSRL) to 2.0 Å at -178°C
15   on a MAR imaging plate at a wavelength of 1.08 Å on beam-line 7-1. The diffraction coordinate data (corresponding to atomic coordinates monomer 1, the other monomer coordinates are provided by matrix conversion of these coordinates, as presented herein) was processed and reduced using MOSFLM version 5.2 from the CCP4 program package (SERC (UK) Collaborative Computing Project 4, Daresbury Laboratory UK, 1979). The program REFIX (Kabsch (1993), *infra*) was used for auto-indexing. Using the CCP4 program suite (SERC (UK) Collaborative
20   Computing Project 4, Daresbury Laboratory UK, 1979), the intensities were scaled (ROTAVATA), merged (AGROVATA) then converted to amplitudes and truncated with the program TRUNCATE. Statistics of the data collected are given in Table 1. The V_m (Matthews, B.W., *J. Mol. Biol.* 33:491-497 (1968)) is 3.2 Å³/Da for 2 monomers in the asymmetric unit, corresponding to a solvent content of 62%.

  Molecular Replacement

25   *Search Model:* The best molecular replacement results were obtained using a multi-Ala core as a search probe. The 'multi-Ala core' search model was constructed from the atomic coordinates of the CPW monomer (Liao et al., 1992), based on the sequence alignment as presented in Figure 15. Regions expected to deviate in structure between PPCA and CPW were deleted from the model (i.e. with low sequence identity or located in loops). The 125 residues identical in PPCA and CPW were left in the model; 112 residues were truncated to alanine. The remaining 94 residues through
30   differing between CPW and PPCA, were considered sufficiently similar in size and the CPW residue left as such in the model. The resulting 'multi-Ala core' monomer consisted of 331 residues, constituting a large portion of the core domain and little atomic information for the 'cap' domain (see Figure 1). The model contained 30% of the expected protein scattering mass given the fact that there are two monomers in the asymmetric unit. The sequence identity between this search model and the true PPCA structure was 37.7%.

35   *Rotation Function, PC Refinement and Translation Function:* Native data of 8 - 4Å was used in the molecular replacement calculations. The rotational searches utilized a real space Patterson search method, as implemented in X-PLOR (Steigeman, 1974; Huber, 1985, Brünger 1992a) with a Patterson vector cutoff of 21Å. The self-rotation function failed to reveal any non-crystallographic two-fold symmetry relating two monomers in the asymmetric unit. In addition, the native self Pattersons did not reveal the presence of a non-crystallographic two-fold
40   axis parallel to a crystallographic axis. These results indicated that the two monomers in the asymmetric unit might not form a dimer together. The cross-rotation function was carried to find the orientation of the two monomers in the asymmetric unit as follows. Patterson vector sets were calculated for the search model and the native data and the 8000 strongest Patterson vectors were used in the rotation function. The rotational space restricted to the asymmetric unit of the rotation function according to Rao et al., 1980, was sampled by rotating the Patterson vectors from the search model
45   around Eulerian angles θ1, θ2, and θ3, while sampling θ2 in angular grid intervals of 2.5°. The 5000 highest rotation

function grid points were selected resulting from the product function of the two Patterson vector sets. The grid points (differing less than 8° around any given axis) were then clustered. The result was a list of 169 possible solutions for the rotation function, each corresponding to a set of three angles describing an orientation. The two top solutions were 3.9 and 3.8 sigma above the mean. PC-refinement (Brünger, 1990) was carried out to optimize each of the 169 possible
5 solutions using the complete search model as a single rigid body. This yielded two orientations with a PC-index of 0.043 and 0.051 respectively. The orientations of these solutions were $(D_1 = 261.4, D_2 = 36.22, D_3 = 147.28)$; and $(D_1 = 18.52, D_2 = 47.40, D_3 = 23.22)$, respectively. In contrast, the rest of the possible solutions yielded an average PC-index of 0.022.

Individual translation function calculations were performed on a 1 Å grid. A translational solution was found
10 for each orientation at positions (x=33.30, y=51.97, and z=12.79) and (x=25.23, y=28.58, and z=22.02), with respect to the crystallographic center, as 7.7 and 8.8σ, respectively, above the mean. The R_{factor} for the individual solutions was 55.6% and 54.8% in the resolution range 8.0 to 4.0Å, with a correlation coefficient (CC) of 0.095 and 0.114. A combined translation function was calculated to place each solution relative to the same crystallographic origin, resulting in an R_{factor} of 52.8% for data between 8.0 and 4.0Å, bringing the R_{factor} down to 51.3% and increasing the CC to 0.22.
15 The molecular packing was assessed on a graphics workstation, which revealed no clashes between the placed search probes. However, a very large amount of empty space was present. The packing showed that the asymmetric unit contained two half dimers, each forming a dimer with another monomer in a neighboring unit cell. The two cores in the asymmetric unit were related by κ=73° around an axis tilted 15.5° off the crystallographic a axis lying in the a,c plane.

20 *Iterative Model Building and Two-fold Averaging*

Initial Electron Density Map: A $2m|F_{obs}| -D|F_{calc}|$ SigmaA weighted map (Read, 1986) was calculated using $|F_{calc}|$'s and phases from the molecular replacement solution. The map was contoured at 1σ and showed good density for most of the core. Density emerged for many side chains where the input model residue had been an Ala, indicating that the molecular replacement solution was correct.

25 *First Model Built:* The two rotated and translated search probes formed the starting point for model building of the PPCA precursor. The non-crystallographic symmetry (NCS) matrix was determined between the two cores using the "Lsq_explicit" option in the computer program O (Jones et al., 1991). Subsequently a 'best monomer' was built by superimposing the electron densities from each monomer core, and adjusting the model accordingly. Residues were only incorporated in the model where the electron density was visible for the complete side chain. Residues from the search
30 model for which no density was visible were removed. An alanine was built in the model at places where electron density for a side chain was partial. In this manner 294 residues, i.e. 65% of the C^α atoms were built in the 'best monomer' core. The second monomer was generated from the 'best monomer' model using the NCS operator relating the two monomers in the asymmetric unit. At this point the data set was partitioned in a working set and a test set consisting of 5% of the reflections between 8 - 2.2Å to monitor the R_{free} (Brünger et al. 1992b). The working data set
35 was used for rigid body and positional refinement. For averaging and map calculations the unpartitioned data set was used. Twenty-five cycles of refinement using the two 'best monomers cores' positioned in the asymmetric unit as rigid bodies and data from 8.0 - 3.0Å, resulted in an R_{factor} of 53.5% for this resolution range. The atomic coordinates of this partial model were used to calculate a new $2m|F_{obs}| - D|F_{calc}|$ SigmaA weighted map which we called the 'best monomer map'.

40 *Averaging: Search for Missing Density:* The phasing power from the rigid body refined 'best monomer cores', consisting of 294 residues per core was insufficient to bring back interpretable electron density for the missing part of the model, 158 residues per monomer. To overcome this a 'bootstrapping' procedure was applied, entailing density averaging using RAVE (Kleywegt & Jones, 1994a) and model expansion. The 'best monomer map' and the rigid body refined 'best monomer cores' served as the starting point for this procedure.

Six bootstrapping cycles were carried out, called bmc1 through bmc6, allowing for the model to be extended in stepwise increments. Figure 16 shows a scheme of the steps incorporated in one bootstrapping cycle. After a cycle in which the model had undergone major expansion, a new molecular mask was calculated with MAMA (Kleywegt & Jones, 1994b) for use in the subsequent bootstrapping cycle. No phase recombination was applied between bootstrapping cycles. At the end of each cycle the inverted phases α_{inv} and inverted amplitudes F_{inv}'s were discarded. The NCS operator was re-optimized after cycle bmc3. The resolution range of the data included in the bootstrapping cycle started with 15 - 3.0 Å for bmc1 and was gradually extended to 15 - 2.7 Å in bmc6. The bootstrapping procedure is summarized in Table 2. To optimize the bootstrapping procedure, consideration was given to the molecular mask used in the averaging, the model building strategy and the refinement procedure.

Molecular masks: Four different masks were constructed in total. The atomic radius of all atoms was set to 4Å to calculate each mask. The masks were then manually modified using mask editing options in O (Jones *et al.* 1991). Mask1, was constructed around the 'best monomer core'. Subsequently it was greatly enlarged by multiple blocks of 10 - 15 Å³ in the regions where the model was incomplete (Figure 17). This was crucial to prevent the density in the insertion area's from being flattened during the averaging step. Approximately one half of the dimer interface was estimated to be formed by regions from the missing cap domain. Major expansions of the mask in this area were made to accommodate for this. This resulted in a serious overlap problem when the mask was duplicated to cover a complete dimer. The mask was reduced where overlap occurred with the "overlap_trim" option of MAMA. After several bootstrapping cycles, new incorporated polypeptide fragments were carefully assigned to one of the two monomers forming the dimer and the mask at the dimer interface area's was manually adjusted accordingly. Essentially the masks were kept far too large in regions where the model was missing in order to avoid erroneous flattening of electron density. In contrast the masks were tightened around the area's of the molecule where the model was complete.

Model Building: A conservative model building strategy was adopted. Initially only side chains were mutated in the core region to fit the PPCA amino acid sequence and where the density was clear, poly-alanine fragments were built in the insertion area's (loops and the cap domain). Newly included atoms were given a B-factor of 20 Å². Only once models bmc5 and bmc6 were obtained, was the electron density of sufficient quality to allow side chains to be incorporated confidently in the cap domain (residues 190 - 303). At this stage the C$^\alpha$ trace was virtually complete for the whole dimer and the sequence could be fit unambiguously.

Refinement: Positional refinement was postponed until after 3 cycles of bootstrapping resulting in a final model containing 91% of the C$^\alpha$ atoms. Forty steps of positional refinement were then carried out to improve the geometry of the model. Subsequently only one of the refined monomer was taken and the other generated using NCS operators. The rational for delaying the positional refinement is addressed in the discussion.

Completing the model: deviations from two-fold symmetry. It was possible to add 148 residues and 185 side chains per monomer after a total of 6 bootstrapping cycles. At this stage, each subunit contained 442 residues and 413 side chains, i.e. 98% of the C$^\alpha$ and 91% of the side chains atoms. The gradual model expansion as a function of the bootstrapping cycle is shown in Figure 18.

Twenty residues were still missing in the asymmetric unit at this stage. These were localized to two stretches per monomer (260 - 262 and 287-292). With most of the scattering mass incorporated, the monomers from model bmc6 was refined individually with X-PLOR (Brünger, 1992a) in an attempt to retrieve electron density for the still missing residues. After 40 steps of positional refinement using data from 8.0 - 2.6 Å, the R_{factor} dropped significantly from 40.2% to 33.2%. The model was further positionally refined using a full weight W_A on the crystallographic term. The data included in the refinement was gradually extended to 2.2 Å. At 2.4 Å resolution individual B-factors were refined and the distribution checked as a function of atom location (*i.e.*, low B-factors in the core and high B-factors on the surface). Cycles of refinement and refitting allowed for 18 missing residues to be added. Essentially almost the complete cap domain was retrieved using the bootstrapping procedure, as shown in Figure 19. It became apparent from the refined maps that the two stretches of missing amino acids adopted a very different conformation in the two monomers (with

as much as an average r.m.s.d. of 7.9 Å for the C"s of residues 287 - 292). For this reason electron density for these regions had not been retrieved in the two-fold averaging process. The stepwise improvement of the electron density maps along with averaging, model expansion and refinement is shown in Figure 6.

The program ARP was used to check our model, in particular the region at the dimer interface (Lamzin &
5   Wilson, 1993). Prior to the final round of positional refinement, an IF$_{obs}$I/σ cutoff was applied to reject 10% of the weakest data as well as an anisotropic scale factor to offset the decreased resolution along the crystallographic a axis. The final model is of good geometry with a final R$_{factor}$ of 21.3% (R$_{free}$ of 26.8 %) for data between 8.0 and 2.2 Å (see Table 3). A Ramachandran plot is given in Figure 21. The r.m.s. coordinate error is 0.282 as calculated by SigmaA (Read, 1986). The average phase difference between the initial molecular replacement model and the currently refined
10 model is calculated to be 71° for data between 10 - 2.2 Å.

The structure determination of PPCA is special in that two-fold averaging could be applied to refine very poor molecular replacement phases, enabling us to retrieve electron density for 148 residues and 185 side chains per monomer. In total 314 complete residues were added per asymmetric unit, equivalent to about 35 kDa of protein. In retrospect we feel that a number of factors contributed to a successful structure determination.

15   *Crystal Packing.* Each monomer in the crystal is interacting with four non-crystallographically related monomers. By far the most extensive contact is with a non-crystallographically related monomer generating the physiological dimer. Three additional contacts are extensive crystal contacts ranging from 200-800 Å² averaged per monomer. The largest nondimer crystal contact involves the precursor loops from two crystallographically independent monomers (region 265-267, 281-295 from monomer 1 with residues 281-293 from monomer 2) making intimate contact
20 with each other. Summed together these loops create an intermolecular buried surface of 1680 Å². We believe that this stabilizes an otherwise very flexible area, possibly explaining the good diffraction qualities of the P2$_1$2$_1$2 crystals.

It is also in this crystal contact that we find deviating spacial conformation and secondary structure between the two monomers as mentioned before. The electron density in this region is of very good quality with average temperature factors of 16.6 Å² for main chain and 18.3 Å² for side chains.

25   *pPPCA and the Hydrolase Family.* The fold of pPPCA belongs to the large hydrolase fold family containing enzymes such as the serine carboxypeptidases, dehalogenase, various lipases and acetylcholine esterase (Ollis *et al.* (1992), *infra*), having various different catalytic functions. Though the central core is the same (a central β-sheet flanked by α-helices on both sides) the proteins in this family all seem to have different 'cap' domains, both with respect to fold as well as size (Figure 7A-F). pPPCA has one of the largest cap domains comprising 121 residues forming the three
30 helical bundle of the helical subdomain and a three stranded β-sheet of the maturation subdomain.

Major Differences and Comparison With the Serine Carboxypeptidases. The overall fold of the pPPCA monomer is similar to that of the wheat and yeast serine carboxypeptidases (Endrizzi *et al.* (1994), *infra*; Ollis *et al.* (1992), *infra*). The complete core domains of pPPCA and CPW superimpose with an r.m.s. deviation of 1.7 Å for 302 Cα atoms and 38% sequence identity. Deleting major deviating loops from the core domain allows for pPPCA to
35 superimpose with an r.m.s. deviation of 1.2 Å onto CPW and CPY (293 equivalent C"s with 40 % sequence identity for CPW/pPPCA and 271 equivalent C"s for CPY/pPPCA with 42.2% identity).

The cap domain in pPPCA differs significantly from the CPW and CPY counterparts. The pPPCA structure reveals a large maturation subdomain not present in the structure of CPW and CPY for which the structures of the enzymatically active forms are known. All three enzymes contain a 3 helical bundle in the cap domain. The sequence
40 identity between the three proteins in this region is very low (ca. 12 %). In contrast, PPCA shows a much greater deviation. Hα1 superimposes reasonably well with the CPW counterpart maintaining the same general orientation with respect to the core domain (requiring a rotation of only 7.4°). But helices Hα2 and Hα3 have undergone major rotations with respect to Hα1 and the core domains by κ = 28.5° and κ = 93.4°, respectively (Figure 8A).

Due to the integral role of the cap domain in forming the dimer interface, the dimers of PPCA and CPW were
45 compared. In the pPPCA and CPW dimers the monomers are oriented differently with respect to each other.

Superposition of the core domain of one monomer from each dimer shows that the second pair of monomers (forming the respective dimers) differ by a remarkable 15° in orientation (Figure 8B). Thus. it appears that the extensive differences in the cap domains lead to a different arrangement of the subunits in the dimers of PPCA and CPW.

Catalytic Triad and Enzymatic Mechanism. Our structure shows that the precursor PPCA has all the elements
5   proposed for the enzymatic machinery of the serine carboxypeptidase family (Liao *et al.* (1992), *infra*: Endrizzi *et al.* (1994), *infra*), and is now discovered to be the third structure elucidated belonging to this family of enzymes after CPW and CPY. The catalytic triad in the active site of pPPCA is formed by residues Ser 150, His 429 and Asp 372. The O^γ of Ser 150 forms a good hydrogen bond with the $N^\epsilon 1$ of His 429 with a N to O distance of 2.8 Å. The $N^\delta 1$ of His 429 is 2.7 Å removed from the $O^\delta 2$ and 3.3 Å from the $O^\delta 1$ of Asp 372. Further, two backbone amides appear to orient the
10 carboxylate group of Asp 372. The N of Ala 374 is at a distance of 3.0 Å to the $O^{\delta 1}$ of Asp 372 and the N of Cys 375 is at a distance of 2.9 Å to the $O^{\delta 2}$ of Asp 372.

The oxyanion hole proposed to stabilize the negatively charged tetrahedral intermediate in serine carboxypeptidases is formed by the backbone amides of Gly 57 and Tyr 151 in PPCA. The 32 atoms of the catalytic triad residues plus the oxyanion hole amides from PPCA, CPY and CPW superimpose with an r.m.s. deviation of 0.4
15 Å indicating the very high degree of structural similarity of the active site in the PPCA precursor with those in the fully active enzymes CPY and CPW, (see Table 4). The carboxylate of Asp 372 and the imidazole of His 429 in PPCA are non-planar, making an angle of approximately 60° between the imidazole and the carboxylate. A similar non-planarity has been observed in CPW and CPY, in contrast to the planar orientation found in subtilisin-.and trypsin-type serine proteases (McPhalen *et al.*. *Biochemistry 27*:6582-6598 (1988)).

20 In pPPCA, a pair of glutamic acid residues (Glu 69 and Glu 149) is positioned near the catalytic triad, with their carboxylate groups interacting with each other. The carboxylate groups are located at approximately 8 Å from the O^γ of Ser 150, and lie at the bottom of the active site. An asparagine (Asn 55) is orientated such that it forms a hydrogen bond to each of the two carboxylate groups of the glutamic acid pair, at an $N^{\delta 2}$ (Asn) to $O^{\epsilon 1}/O^{\epsilon 2}$ (Glu) distance of 3.0 and 3.6 Å, respectively. In addition the two carboxylates interact with each other via hydrogen bonds. This configuration
25 of two glutamic acid residues and an asparagine, is conserved between pPPCA, CPW and CPY (see Table 4), and has been implicated in regulating the low pH optimum for the carboxypeptidase activity found in the serine carboxypeptidases (Liao *et al.* (1992), *infra*). Biochemical data has suggested that a functional group with an apparent pK_a value of pH 5.5, functions to bind the C-terminal carboxylate group of peptide substrates and is responsible for the observed pH optimum of 5.5 (reviewed in Breddam *et al.* (1986), *infra*; Rawlings & Barrett (1994), *infra*). Together
30 with their structural data, Liao and colleagues (Liao *et al.* (1992), *infra*) have suggested that at pH 5.5 or below. one or both glutamates must be uncharged, while at a pH higher than 5.5 one or both of the carboxylates which are orientated opposite to each other, may become deprotonated resulting in unfavorable electrostatic interactions. This would disturb the hydrogen bonding pattern or result in structural perturbations causing the observed increase in K_m for peptide substrates at high pH. In pPPCA the orientation of this pair of glutamic acids as well as that of the asparagine is
35 essentially identical in structure to the equivalent residues in CPW and CPY (see Table 4). even though the structure has been determined at pH 8. The CPW and CPY structures have been determined at pH 5.7 and at pH 6.5-7.0. Thus, our structure appears to rule out large pH induced conformational changes of these three residues at least up to a pH value 2.5 units above that optimal for carboxypeptidase activity. However the high degree of conservation of these residues does indicate some role in a characteristic shared by all three enzymes.

40 From our comparison it is clear that the enzymatic machinery in the PPCA precursor form is in a conformation virtually identical to that found in the fully active CPW and CPY enzymes. On this basis, the conformation of the enzymatic machinery found in pPPCA is expected to faithfully represent the conformation that will be found in the active PPCA.

Active Site, Substrate Specificity. PPCA has a substrate preference for hydrophobic residues in the P1 and/or P1' binding pockets (Jackman *et al.*, *Hypertension 21*:925-928 (1993)). In CPW the P1' pocket was identified to consist of two tyrosine residues (Tyr 60 and Tyr 239) which form a long channel, capped by two acidic residues (Glu 272 and Glu 398) at the end (Liao *et al.* (1992), *infra*). This explains the highest preference of this enzyme for Arg and Lys as

5 the leaving group (Breddam *et al.*, *Carlsberg Res. Commun. 52*:297-311 (1987)). In CPY a similarly shaped pocket is formed by the residues Thr 60, Tyr 256, Leu 272 and Met 398 (Endrizzi *et al.* (1994), *infra*). In PPCA the analogous residues are Tyr 247 and Asp 64, forming the sides of the pocket with at the far end Met 430 and Thr 304. This is reasonably consistent with an overall preference of PPCA for a hydrophobic leaving group.

Inactivation Mechanism of the Precursor Form. During the maturation step of the PPCA precursor form, at

10 maximum residues 285-298 forming the 'excision' peptide, are removed by an as yet unidentified protease(s). *In vitro*, the maturation event can be mimicked by digestion with trypsin utilizing probably positions Arg 284, as well as Arg 292 and/or Arg 298. The residues forming the 'excision' peptide adopt distinctly different conformations in the two crystallographically distinct monomers forming the PPCA dimer in our crystal structure. Yet in both monomers this polypeptide region extends out from the protein surface and is virtually completely solvent and protease accessible

15 (Figure 9). Arg 284 and Arg 292 are particularly well exposed. The main chain atoms of Arg 298 are less accessible, being sandwiched between the strand Mβ2 and a loop N-terminal to helix Cα6, while a salt bridge with Glu 264 renders the side chain atoms of Arg 298 partially solvent inaccessible.

The active site cleft is blocked by numerous residues from the maturation subdomain in the precursor form of PPCA. The catalytic triad is rendered solvent inaccessible by residues Asn 275, Ile 276 and Phe 277. These residues

20 are part of the polypeptide Asp 272-Phe 277 which we call the 'blocking' peptide. This peptide is held down predominantly by hydrophobic contacts of Leu 273, Ile 276, and Phe 277 to the core domain residues Gly 57, Cys 60, Leu 180, Leu 190, Val 191, Leu 232, Val 235, Ile 246, Leu 280, Leu 282, Met 299 and Ala 373 (Fig 10). In addition residue Asn 275 of the blocking peptide appears to fill what might be part of the P1 binding pocket in the mature form. Further inspection of the blocking peptide suggests that Gly 274 with Ramachandran angles $\phi = 66°$ and $\phi = 28°$, might

25 play a central role in the strand blocking the active site. A glycine at this position appears critical to allow the polypeptide chain to adopt a conformation with its main chain at a safe distance from the catalytic triad. This might aid in allowing the blocking peptide to assume a conformation resistant to autocatalysis. The P1' binding pocket seems to be beautifully filled by Pro 301 interacting with Thr 304, Tyr 247, Cys 60 and Cys 334. Thus substrate binding is not possible in the precursor form due to the inaccessibility of the substrate binding pockets.

30 We conclude that the inactivation mechanism of PPCA is based on blocking of the active site, and not upon changes in the position of functional groups involved in catalysis/transition state stabilization. Both the P1, P2 and P1' binding pockets are rendered solvent inaccessible. The function of the blocking peptide seems to be to render the catalytic triad as well as the region around the P1 and P2 binding pockets solvent inaccessible. The blocking peptide, however, does not assume a conformation that a peptide substrate would adopt. It is carefully positioned in a manner

35 which is different from that of a productive substrate, thereby avoiding being by the nearby catalytic residues which are correctly poised for catalysis. A crucial observation is that the excision peptide itself does not bind in the active site cleft. Hence, mere removal of the excision peptide alone is not sufficient to allow solvent or substrate access to the active site.

Proposed Maturation Event and Extent of Conformational Rearrangement. The active site of the precursor

40 of PPCA appears to be fully blocked by 49 residues of the maturation subdomain, as shown in Figure 11. Based on the precursor structure and the comparison with CPW and CPY it is proposed that a region comprising approximately residues 254-284 rearranges to free the P1, P2 binding sites, while the residues 299-302 rearrange to free the P1' binding pocket. The linker connecting these two segments of polypeptide chain is the 14 amino acid excision peptide Met 285-Arg 298. The extent of the residues rearranging is likely to be limited by a disulfide bridge Cys 253 and Cys 303, which

is conserved in the serine carboxypeptidase family. This critical disulfide serves to keep the secondary structure elements together at the far end of the PI' pocket.

An interesting pair of salt bridges is observed between Arg 262, Asp 300, Glu 264 and Arg 298, four residues located on strands Mβl and Mβ3 of the mixed β-sheet found in the maturation subdomain. This cluster of residues is strategically positioned at the base of the excision peptide, close the core domain and 'shielding' the mixed β-sheet via side chain interactions (see Figure 11). These residues are strictly conserved among the human, mouse and chicken PPCAs (Galjart et al. (1991), infra). This charge cluster may be effected by a shift from neutral to acidic pH. Arrival in the endosome/lysosome is expected to result in protonation of either the Asp or the Glu residue or both, resulting in unfavorable electrostatic interactions and destabilization of this charge cluster. This in turn is expected to promote partial unfolding of maturation subdomain, allowing easier access to additional potential cleavage sites, and stimulating removal of the 'blocking' peptide which fills the active site in the precursor.

A similar double salt bridge has been observed in the aspartic proteinase zymogen pepsinogen between the proenzyme segment (Arg 8P) and the enzyme (Arg 308, Glu 13, Asp 304).

The maturation mechanism for pPPCA appears to be novel among proteases for which the three-dimensional structure of the zymogen is known. The catalytic triad in the precursor form is in a catalytically competent conformation. Enzymatic activity is prevented by a 'blocking' peptide. The blocking peptide is however different from the excision peptide and does not get excised from the mature enzyme. This leads to the distinct difference with the other known maturation mechanisms in that, after disappearance of the excision peptide, up to 35 residues filling the active site cleft in the PPCA precursor must rearrange to render the catalytic triad solvent accessible (see Figure 12), but do not get cleaved off. Removal of the excision peptide, and possibly a shift to lower pH in the endosome/lysosome, appears to be a trigger for this event. The mechanism does not appear to be autocatalytic, as uptake experiments with cultured galactosialidosis fibroblasts, have shown that a mutant PPCA with the catalytic Ser 150 mutated to Ala, is properly targeted and processed. It retains its protective function and except for the loss of catalytic activity is biochemically indistinguishable from the wild type enzyme (Galjart et al. (1991), infra). Surprisingly, the maturation mechanism of the serine carboxypeptidases PPCA, CPW and CPY may all differ from each other as well. This is clearest for CPY, in which a 91 residue polypeptide is cleaved off N-terminally to convert the zymogen to an active enzyme (Winther and Sorensen, Proc. Natl. Acad. Sci. USA 88:9330-9334 (1991)), as opposed to the excision of a peptide from within the zymogen generating a two chain active form as is the case for PPCA and CPW.

Looking at the hydrolase fold family, the catalytic triad is housed in the core domain and the various cap domains attenuate the biological function by influencing entirely different properties such as: (I) enzyme kinetics exemplified by the interfacial activation of lipases (Smith et al., Curr. Opinion in Structural Biology 2:490-496 (1992)); (ii) substrate channeling as is proposed for acetylcholine esterase (Sussman et al. (1991), infra); (iii) substrate recognition, proposed for dehalogenase by (Franken et al. (1991), infra) and for CPY and CPW by (Endrizzi et al. (1994), infra); and (iv) enzyme inactivation in the case of PPCA.

Biological Implications. Deficiency of the protective protein/cathepsin A (PPCA) in humans results in the lysosomal storage disease galactosialidosis. PPCA is thought to form a multi-enzyme complex with β-galactosidase and neuraminidase in the lysosomes protecting the latter glycosidases in their harsh acidic and proteases-rich environment. PPCA has a 30% sequence identity to the wheat serine carboxypeptidase (CPW) and yeast serine carboxypeptidase (CPY). It has been show that PPCA in the precursor form is inactive, but upon maturation, entailing excision of a 2 kDa peptide, carboxypeptidase activity is released.

The precursor structure reveals an inactivation mechanism that has not been seen before in any of the other known zymogen structures of proteases (available for the serine-, metallo- and aspartic protease classes). The catalytic triad seems to have an arrangement poised for catalysis. However, the triad is rendered solvent and substrate inaccessible by a strand from the maturation subdomain binding in the active site cleft. Surprisingly, this strand called the 'blocking' peptide does not overlap with the 2 kDa 'excision' peptide. Hence, after removal of the excision peptide

up to 35 additional residues must rearrange in order to unblock the active site cleft. A strategically positioned pair of salt bridges. comprising Arg 262, Arg 298. Glu 264. and Asp 300 at the base of the excision peptide. are expected to optionally become destabilized at low pH, unraveling this region of the structure, allowing easier access to cleavage sites and/or promoting the rearrangement event.

5   A number of research groups are currently involved in designing enzyme and gene therapy procedures for several lysosomal storage diseases. Insight into the three-dimensional structure, protein functioning and stability of PPCA. the first enzyme of known structure associated with a lysosomal storage disease and the third human lysosomal structure to be determined. may prove useful in future designs of an adequate therapy procedure for galactosialidosis. Information from the three-dimensional structure of PPCA, might also aid in designing an engineered form of PPCA

10   with increased stability and a longer half-life.

Table 1: X-ray Data Collection Statistics

resolution	32.27-2.2 Å
wavelength	1.08 Å
space group	$P2_12_12$
unit cell	a=115.04 b =148.11 c=80.97 Å
temperature of data collection	-178°C
No. of observed reflections	436,709
No. of unique reflections	67,740
completeness of all data	95.7%
R_{sym} for all data	5.1%
completeness of outer shell (2.26-2.20Å)	87.0%
R_{sym} in outer shell (2.26-2.20Å)	13.0%

$R_{sym} = \sum\sum I_i(h)-<I(h)>/\sum\sum I_i(h)$, where $I_i(h)$ is the ith observation for reflection h and $<I(h)>$ is the weighted mean of all the observations.

Table 2: Course of Model Building

Model	nr. of C^αs	nr. of side chains	V_{mask} (10^4 Å³)	Rfactor	R_{free}	CC	CC_{free}
				{statistics using data between 8.0 and 3.0Å}			
mol. repl. (mr) rigid body ref. (rmr) calculate NCS matrix	331	125	-	54.2 52.6	55.3 52.9	0.243 0.287	0.244 0.318
best monomer (bm) rigid body ref. update NCS matrix	294	228	-	55.9 53.5	57.4 55.0	0.228 0.320	0216 0328
bmc1 (mask 1)	373	258	10.8	49.9	51.3	0.403	0.424
bmc2 (mask 1)	405	277	10.8	48.6	48.4	0.443	0.478
bmc3 (mask 2) rigid body ref. positional ref. (pbmc3) update NCS matrix	411	307	9.99	47.1 46.9 39.4	48.6 48.4 44.7	0.471 0.476 0.622	0.491 0.492 0.562
bmc4 (mask 1)	412	327	10.8	41.7	43.1	0.584	0.585
bmc5 (mask 3)	435	387	8.88	39.8	40.6	0.621	0.623
bmc6 (mask 4)	442	413	9.11	38.4	40.2	0.647	0.637

Summary of the bootstrapping procedure. The resulting models have been listed chronologically starting with the molecular replacement solution, *i.e.* mr (molecular replacement), bm (best monomer core), and the bootstrapping cycles bmc1 through bmc6. The following statistics are given for the various models: the number of C^α atoms built per monomer; the number of correct side chains incorporated per monomer and the volume of the molecular mask used during the averaging if applicable. The quality of each model is assessed using the R_{factor}, R_{free}, CC and CC_{free} calculated by X-PLOR for data between 8.0 and 3.0 Å. After positional refinement of model bmc3, both monomers were made equivalent by taking one monomer and generating the non-crystallographically related one.

Table 3: Current Status of the Model

statistics for the data used in refinement:		
resolution (Å)	Rfactor (%)	completeness (%)
8.0 - 4.3	22.4	85.7
4.3 - 3.5	19.0	89.1
3.5 - 3.0	20.6	89.1
3.0 - 2.8	21.3	87.9
2.8 - 2.6	22.3	86.1
2.6 - 2.4	22.2	84.0
2.4 - 2.3	22.7	81.3
2.3 - 2.2	24.0	78.3
8.0 - 2.2. Å	21.3%	

model:	
molecules in the asymmetric unit:	2
residues (out of 904 possible):	902
sugars:	6
waters:	296

r.m.s.d. bond length (Å):	0.012
r.m.s.d. bond angles (°):	1.72

average B-values for main chain atoms (Å^2):	16.6
side chain atoms (Å^2):	18.3

Table 4

Superposition of the proposed catalytic machinery of the serine carboxypeptidases with known three-dimensional structure PPCA, CPW (Liao *et al.*, *Biochemistry 31*:9796-9812 (1992)) and CPY (Endrizzi *et al.*, *Biochemistry 33*:11106-11120 (1994)).

PPCA		CPW		ΔPPCA-CPW	CPY		ΔPPCA-CPW
Catalytic triad:	N	Ser 146	N	(Å)	Ser 146	N	(Å)
Ser 150	C*		C*	0.3		C*	0.4
	C	His 397	C	0.4	His 397	C	0.5
His 429	O		O	0.3		O	0.4
	C^β		C^β	0.3		C^β	0.4
	O^γ	Asp 338	O^γ	0.9	Asp 338	O^γ	1.1
Asp 372	N		N	1.5		N	0.9
	C*		C*	0.2		C*	0.4
	C		C	0.3		C	0.4
	O		O	0.3		O	0.5
	C^β		C^β	0.5		C^β	0.6
	O^γ		O^γ	0.3		O^γ	0.6
	$C^{\delta 2}$		$C^{\delta 2}$	0.3		$C^{\delta 2}$	0.5
	$C^{\delta 1}$		$C^{\delta 1}$	0.7		$C^{\delta 1}$	0.5
	$N^{\delta 1}$		$N^{\delta 1}$	0.4		$N^{\delta 1}$	0.5
	$N^{\delta 2}$		$N^{\delta 2}$	0.3		$N^{\delta 2}$	0.4
	N		N	0.7		N	0.5
	C*		C*	0.2		C*	0.2
	C		C	0.1		C	0.1
	O		O	0.1		O	0.1
	C^β		C^β	0.2		C^β	0.1
	C^γ		C^γ	0.3		C^γ	0.2
	$O^{\delta 1}$		$O^{\delta 1}$	0.2		$O^{\delta 1}$	0.1
	$O^{\delta 2}$		$O^{\delta 2}$	0.2		$O^{\delta 2}$	0.3
				0.4			0.1
Proposed oxyanion hole (formed by two backbone amides):							
Gly 57	N	Gly 53	N	0.1	Gly 53	N	0.5
Tyr 151	C*	Tyr 147	C*	0.2	Tyr 147	C*	0.4
	C		C	0.1		C	0.4
	O		O	0.3		O	0.8
	N		N	0.3		N	0.2
	C*		C*	0.2		C*	0.1
	C		C	0.3		C	0.2
	O		O	0.5		O	0.2
proposed regulation of pH dependent peptidase activity:							
Asn 55	averaged over all atoms		Asn 51	0.2	Asn 51		0.2
Glu 69	averaged over all atoms		Glu 65	0.3	Glu 65		0.7
Glu 149	averaged over all atoms		Glu 145	0.4	Glu 145		0.4

The residues forming the proposed catalytic machinery are strictly conserved between the three serine carboxypeptidases. The deviation in distance between the atoms from PPCA and the equivalent atoms in CPW or CPY after superposition is given in Angstrom.

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What Is Claimed Is:

1.   A method for crystallizing a human protective protein/cathepsin A (PPCA) or precursor human protective/cathepsin A protein (pPPCA), comprising

(a) providing a purified PPCA or pPPCA;

(b) crystallizing the purified PPCA or pPPCA using a hanging drop or diffusion method, to provide crystallized PPCA or pPPCA having biological activity,

wherein the crystallized PPCA or pPPCA is resolvable using x-ray crystallography to obtain x-ray diffraction patterns suitable for three-dimensional structure determination of the PPCA or pPPCA.

2.   A method according to claim 1, wherein said PPCA or pPPCA has at least one biological activity selected from the group consisting of enzyme protecting activity, enzyme modulating activity and peptide hydrolyzing activity.

3.   A method according to claim 1, wherein said crystallization step is done under conditions of purified PPCA or pPPCA; 2-30% PEG400-10,000; precipitating salt; buffers, and pH 7-9.

4.   A method according to claim 3, wherein the crystallization conditions are PPCA or pPPCA; 5-14% PEG8000, 40-80 mM tromethamine, 0.05-2.0 mM NaN₃ and pH 8.0-8.3.

4.   A method according to claim 3, wherein the crystallization conditions are PPCA or pPPCA; 5-14% PEG8000, 40-80 mM tromethamine, 0.05-2.0 mM NaN_3 and pH 8.0-8.3.

5.   A crystallized PPCA or pPPCA, or at least one subdomain thereof, provided by a method according to claim 1.

6.   A method for providing an atomic model of a PPCA or pPPCA, comprising

(a) providing a computer readable medium having stored thereon atomic coordinate/x-ray diffraction data of said PPCA or pPPCA in crystalline form, said data sufficient to model the three-dimensional structure of said PPCA, said pPPCA, or at least one subdomain thereof;

(b) analyzing, on a computer using at least one subroutine executed in said computer, the atomic coordinate/x-ray diffraction data from (a) to provide data output defining an atomic model of said PPCA or said pPPCA, said analyzing utilizing at least one computing algorithm selected from the group consisting of data processing and reduction, auto-indexing, intensity scaling, intensity merging, amplitude conversion, truncation, molecular replacement, molecular alignment, molecular refinement, electron density map calculation, electron density modification, electron map visualization, model building, rigid body refinement, positional refinement; and

(c) obtaining atomic model output data defining the three-dimensional structure of said PPCA, pPPCA or at least one subdomain thereof.

7.   A method according to claim 6, wherein said computer readable medium further has stored thereon data corresponding to a nucleic acid sequence or an amino acid sequence data comprising at least one structural domain or a functional domain of a PPCA or pPPCA corresponding to a portion of the amino acid sequences of Figures 13 or 14, and wherein said analyzing step further comprises analyzing said sequence data.

8.   A computer readable medium having stored thereon atomic model data of said PPCA or pPPCA as the model output data produced by a method according to claim 6.

9.   A computer-based system for providing atomic model data of the three dimensional structure of a PPCA or a pPPCA, comprising the following elements;

    (a) a computer readable medium having stored thereon atomic coordinate/x-ray diffraction data of said PPCA or pPPCA or at least one subdomain thereof;

    (b) at least one computing subroutine, that when executed in a computer, causes the computer to analyze the atomic coordinate/x-ray diffraction data from (a) to provide data output defining an atomic model of said PPCA or pPPCA, said analyzing utilizing at least one computing subroutine selected from the group consisting of data processing and reduction. auto-indexing, intensity scaling, intensity merging, amplitude conversion. truncation. molecular replacement, molecular alignment, molecular refinement, electron density map calculation, electron density modification, electron map visualization, model building, rigid body refinement, positional refinement; and

    (c) retrieval means for obtaining atomic model output data defining the three-dimensional structure of said PPCA, pPPCA or at least one subdomain thereof.

10.   A computer-based system according to claim 9, wherein said computer readable medium further has stored thereon data corresponding to a nucleic acid sequence or an amino acid sequence data comprising at least one structural domain or a functional domain of a PPCA or pPPCA corresponding to a portion of the amino acid sequences of Figures 13 or 14, and wherein said at least one subroutine further includes analyzing said sequence data.

11.   A computer readable medium, having stored thereon atomic model data of a PPCA, pPPCA, or at least one subdomain thereof, produced by a computer system according to claim 9.

12.   A method for providing an computer atomic model of a ligand of a PPCA or pPPCA, comprising

    (a) providing a computer readable medium according to claim 11, having stored thereon atomic model data of a PPCA, a pPPCA or at least one subdomain thereof;

    (b) providing a computer readable medium having stored thereon atomic model data sufficient to generate atomic models of potential ligands of PPCA or pPPCA;

    (c) analyzing on a computer, using at least one subroutine executed in said computer, the atomic model data from (a) and the ligand data from (b), to determine binding sites of PPCA or pPPCA and to provide data output defining an atomic model of a ligand of said PPCA, pPPCA, or at least one subdomain thereof, said analyzing utilizing computing subroutines selected from the group consisting of data processing and reduction. auto-indexing, intensity scaling. intensity merging. amplitude conversion. truncation, molecular replacement, molecular alignment. molecular refinement, electron density map calculation, electron density modification. electron map visualization, model building, rigid body refinement, positional refinement; and

(d) obtaining atomic model output data defining the three-dimensional structure of a ligand of said PPCA, pPPCA or at least one subdomain thereof.

13.   A computer readable medium having stored thereon the model output data produced by a method according to claim 12.
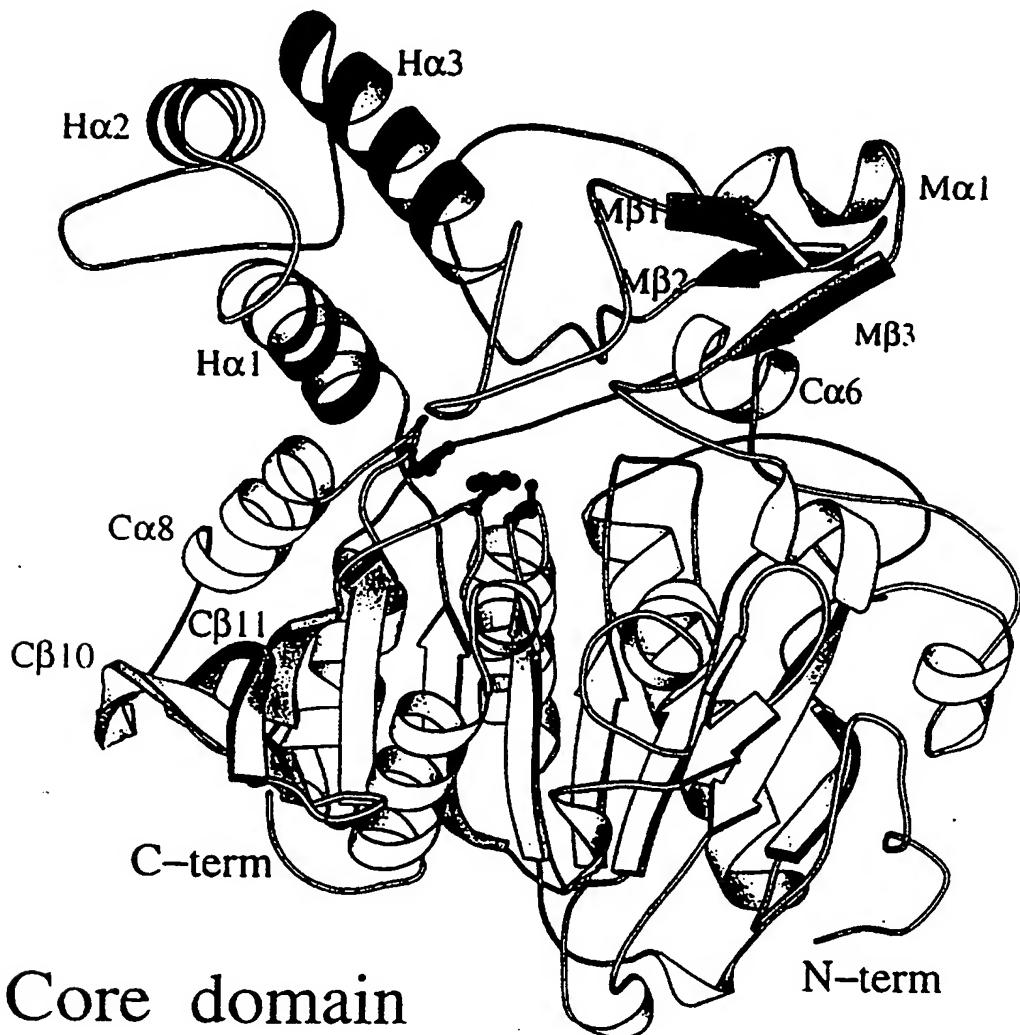
14.   An isolated PPCA or pPPCA ligand, corresponding to the physical molecule of the atomic model of the ligand model produced by a method according to claim 12.

15.   A computer-based system for providing an atomic model of a ligand of a PPCA or pPPCA, comprising the following elements;

(a) a computer readable medium having stored thereon atomic model data of a PPCA or pPPCA;

(b) a computer readable medium having stored thereon atomic model data sufficient to generate atomic models of potential ligands of PPCA or pPPCA;

(c) at least one computing subroutine for analyzing on a computer the atomic model data of PPCA or pPPCA from (a) and the ligand data from (b), to determine binding sites of PPCA or pPPCA and to provide data output defining a atomic models of potential ligands of PPCA or pPPCA, said analyzing utilizing at least one computing subroutine selected from the group consisting of data processing and reduction, auto-indexing, intensity scaling, intensity merging, amplitude conversion, truncation, molecular replacement, molecular alignment, molecular refinement, electron density map calculation, electron density modification, electron map visualization, model building, rigid body refinement, positional refinement; and

(d) retrieval means for obtaining atomic model output data defining the atomic models of potential ligands of PPCA or pPPCA.

16.   A computer readable medium, comprising atomic model output data of a potential ligand of PPCA or pPPCA, said data produced by a method according to claim 15.

17.   An isolated PPCA or pPPCA ligand, corresponding to the physical molecule of the atomic model of a ligand produced by a computer system according to claim 15.

18.   A crystallized pPPCA, having the atomic coordinates presented in Figure 23.1-23.41.
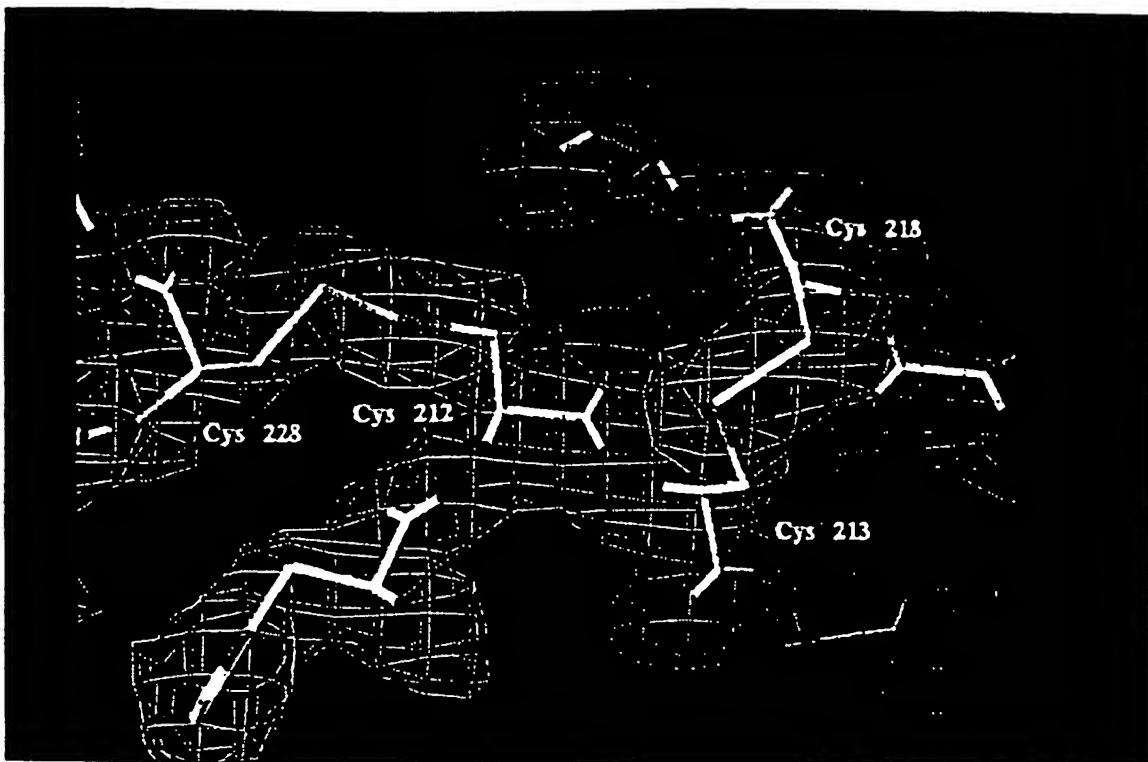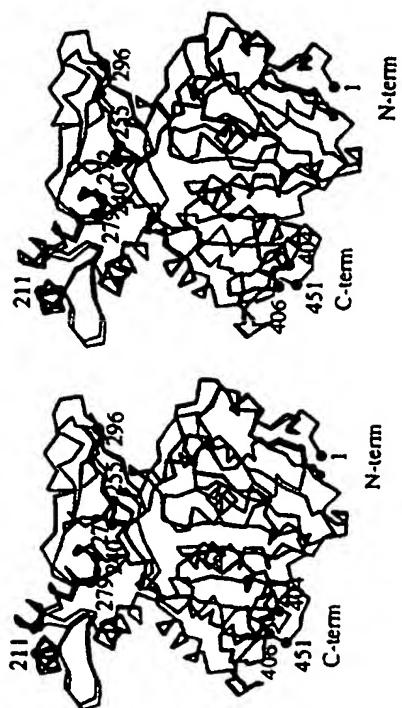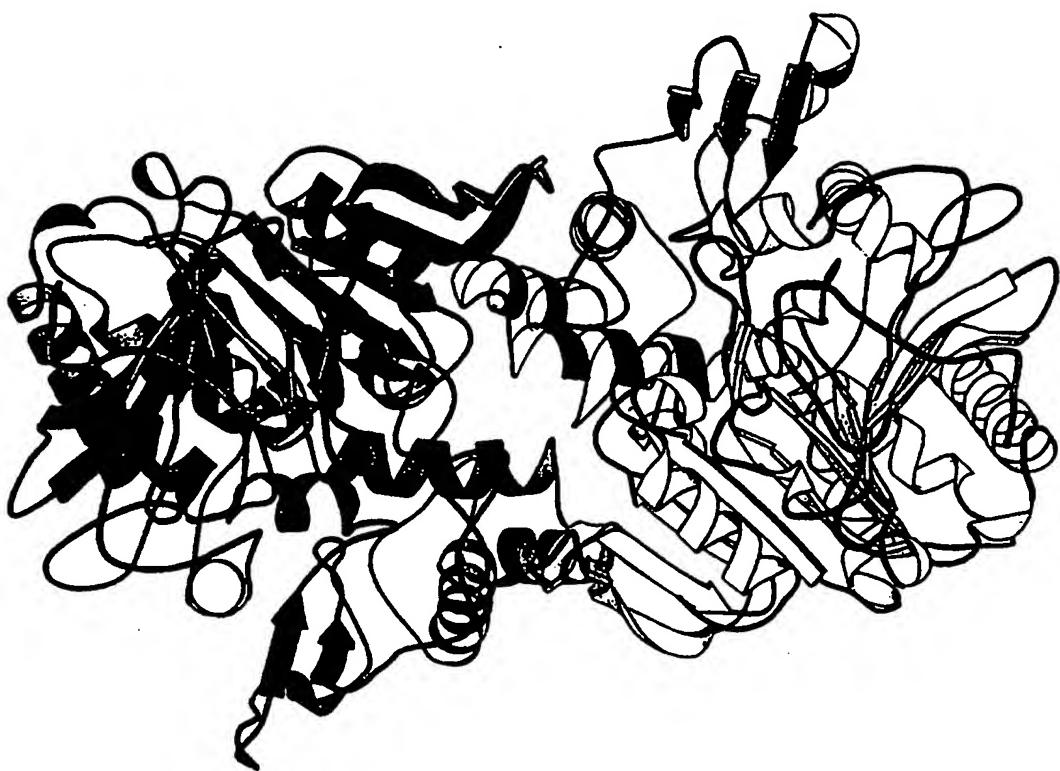
Figure 1

Figure 1

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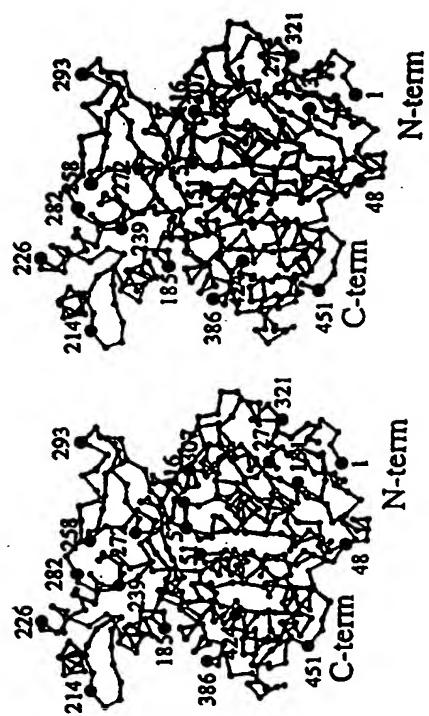
Figure 2

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Figure 3

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Figure 4

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Figure 5

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Figure 6A

Figure 6B

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CPY
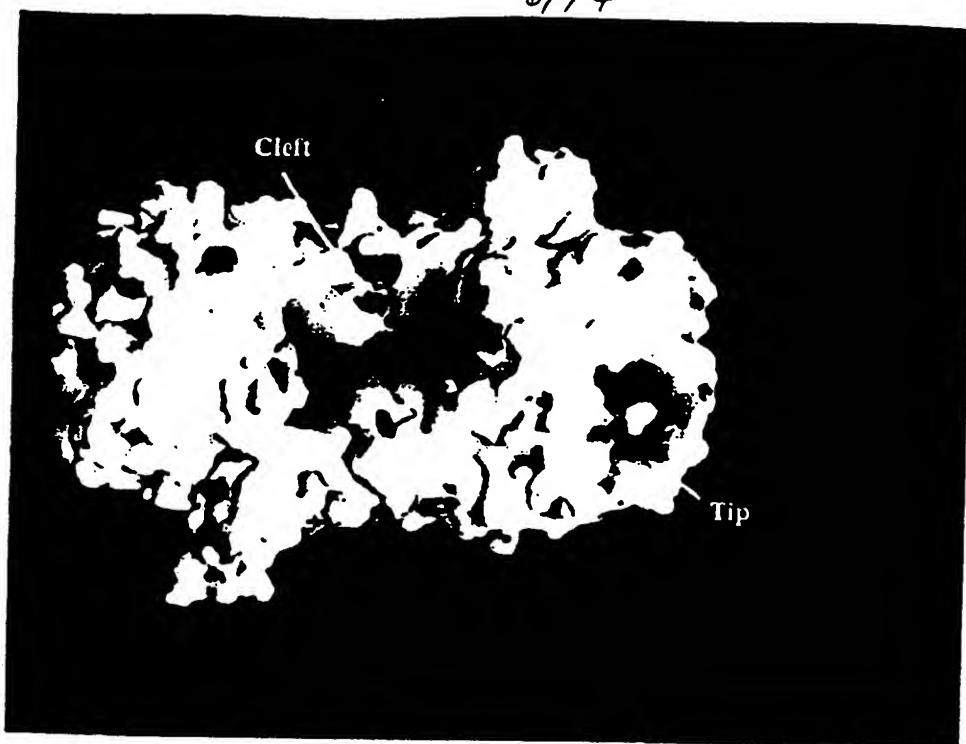
Figure 7C

acetylcholine esterase
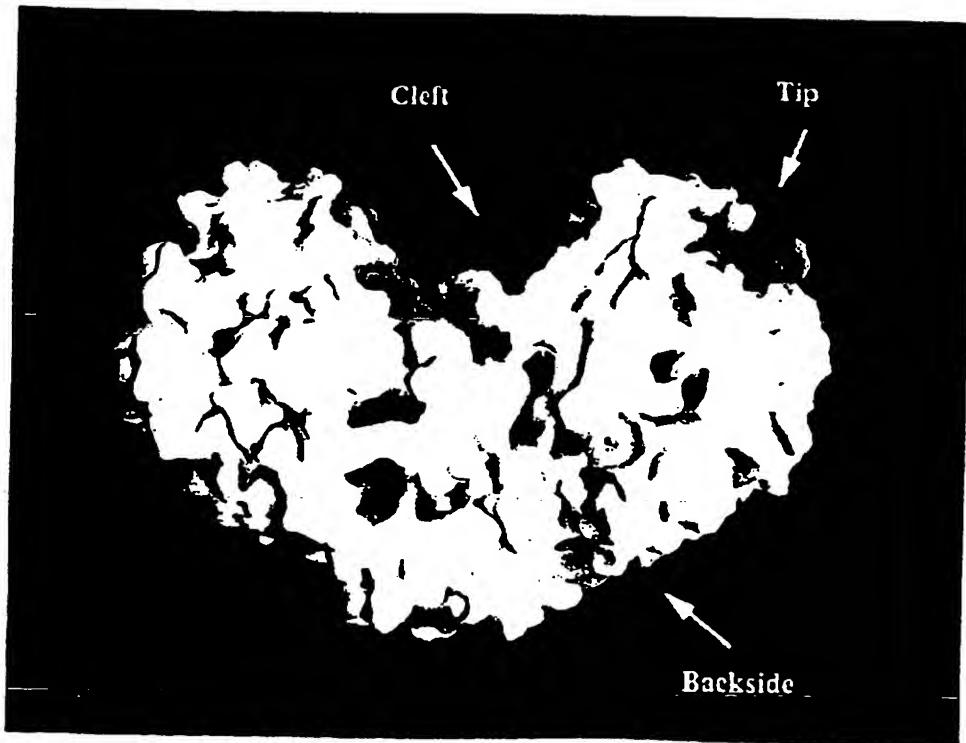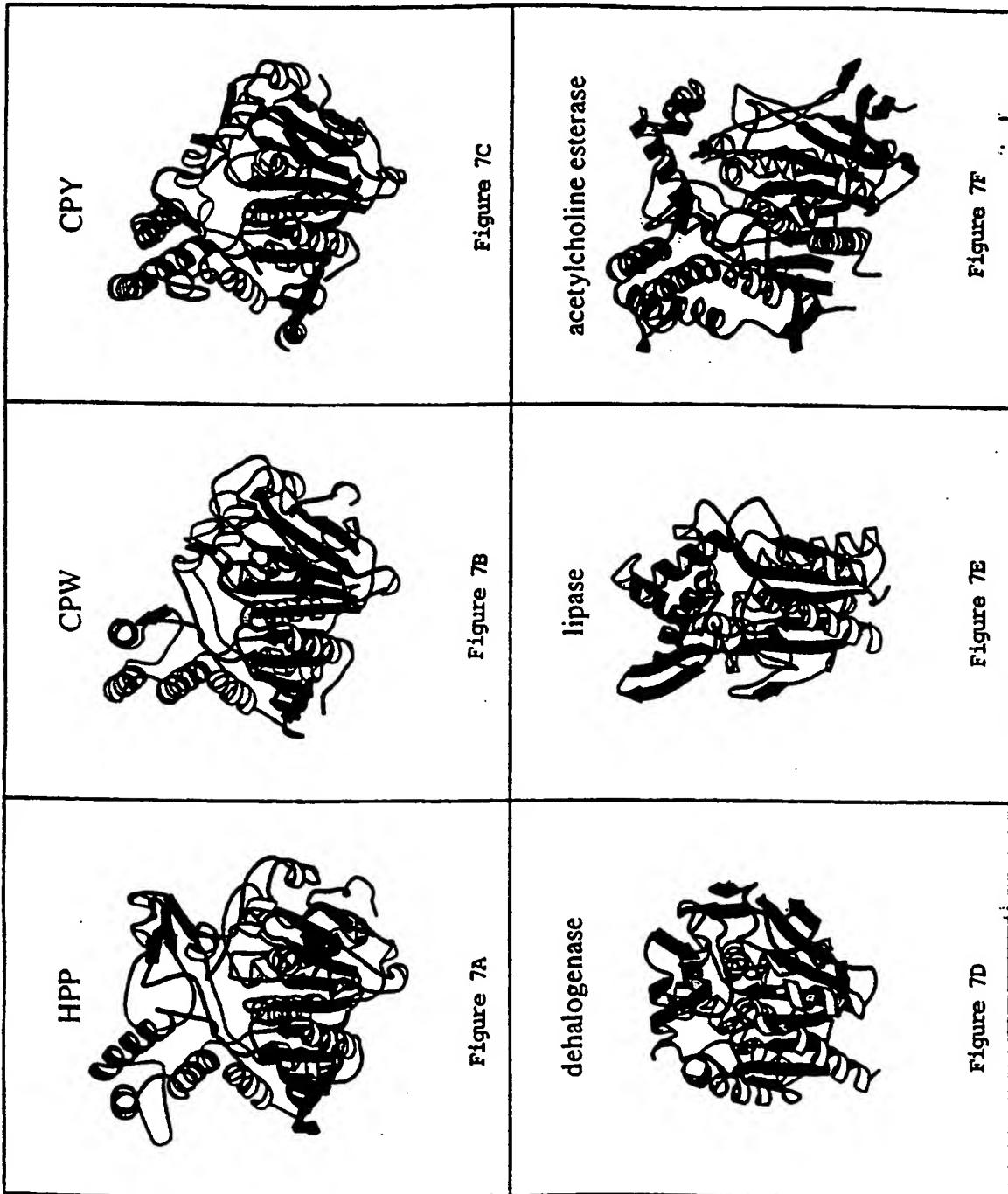
Figure 7F

CPW

Figure 7B
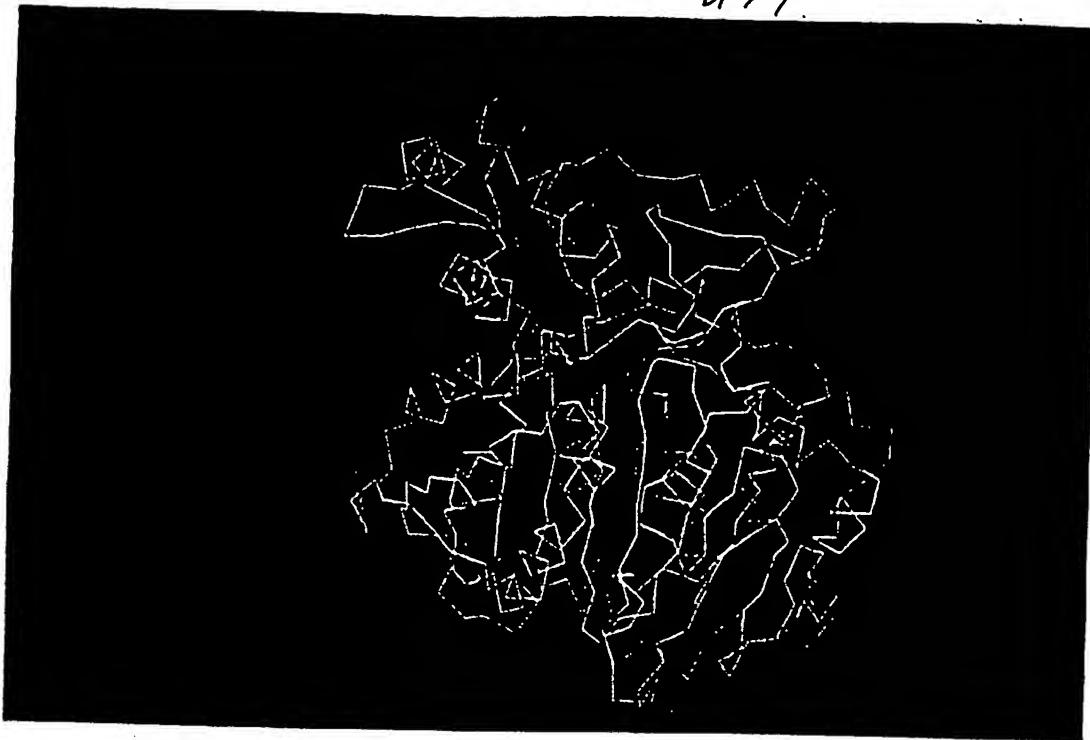
lipase

Figure 7E

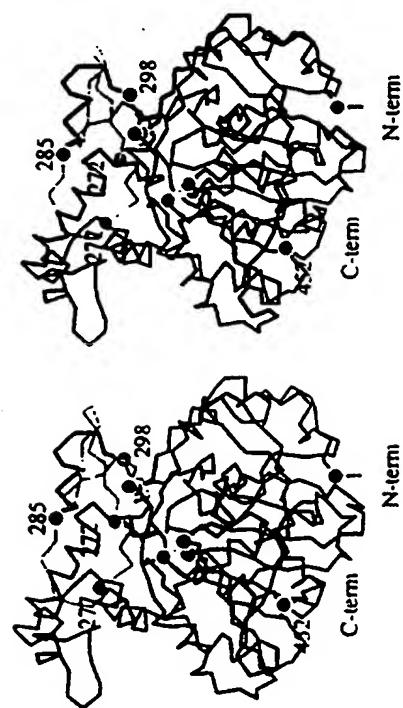HPP

Figure 7A

dehalogenase

Figure 7D
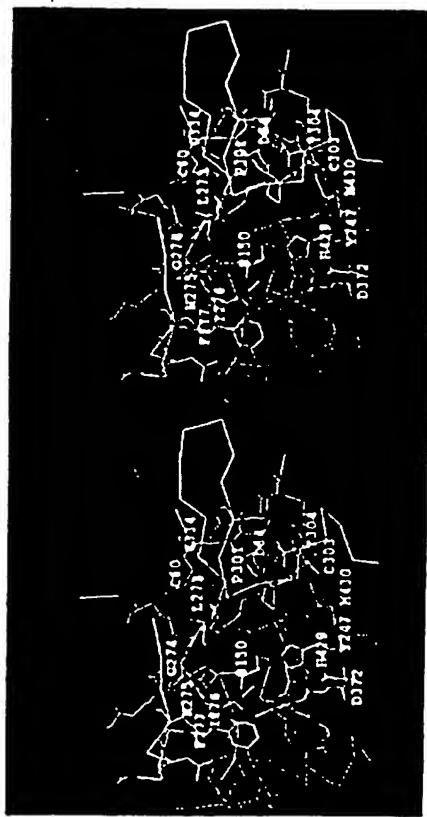
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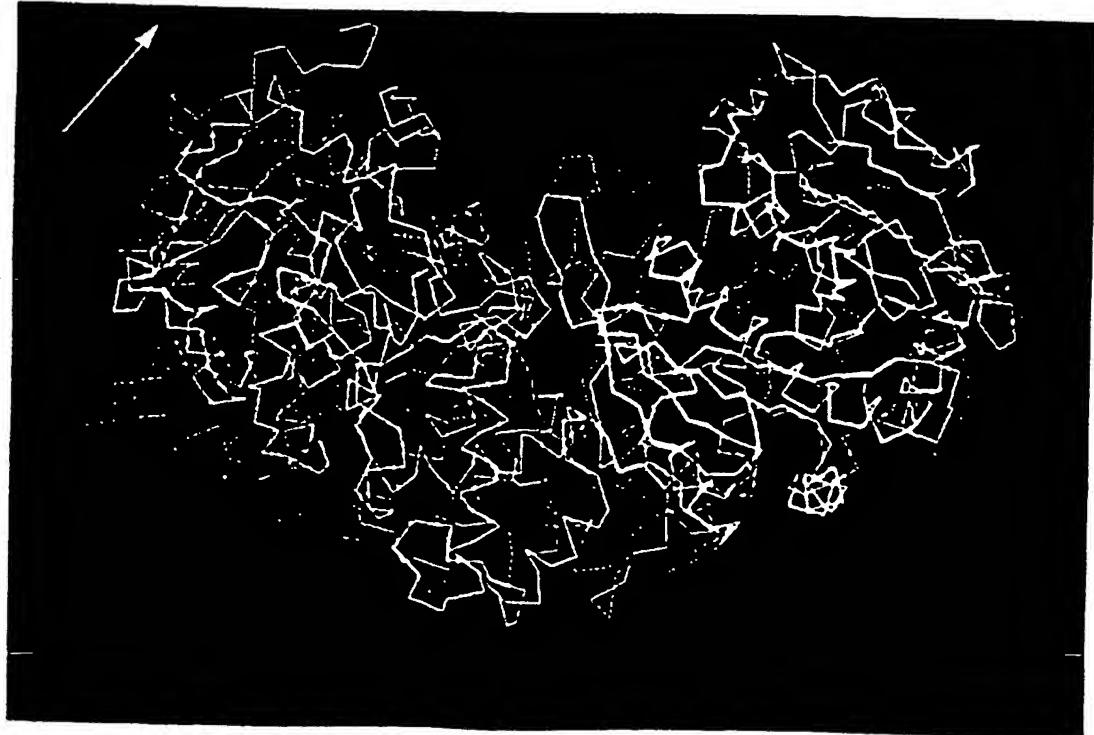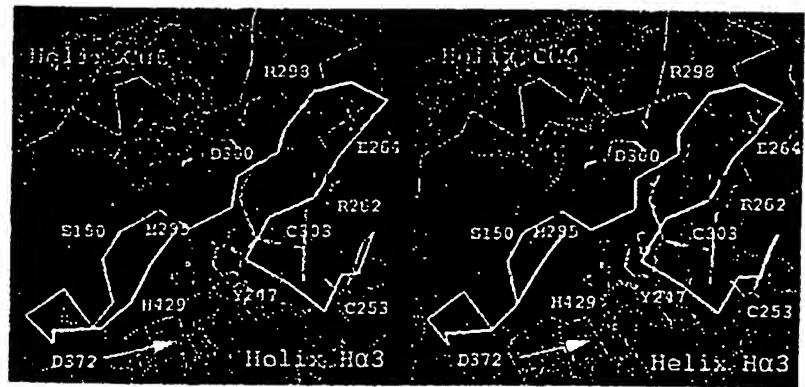
Figure 8A

Figure 8B

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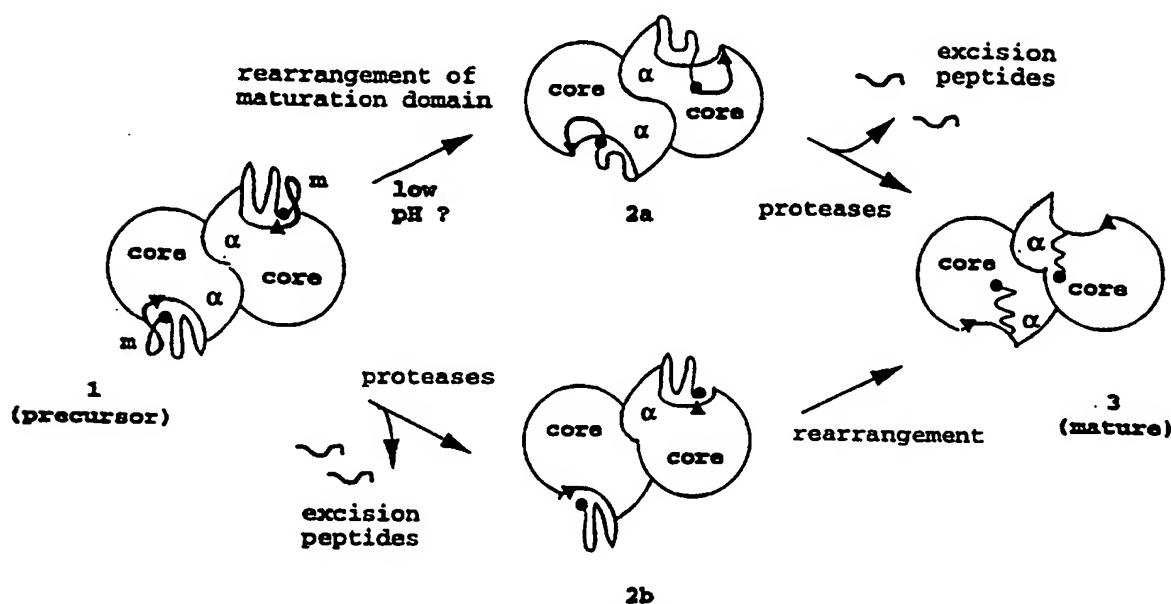
Figure 9

Figure 10

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Figure 11

Figure 12

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1   A P D Q D E I Q R L P G L A K Q P S F R Q Y S G Y L K S S G
31  S K H L H Y W F V E S Q K D P E N S P V V L W L N G G P G C
61  S S L D G L L T E H G P F L V Q P D G V T L E Y N P Y S H N
91  L I A N V L Y L E S P A G V G F S Y S D D K F Y A T N D T E
121 V A Q S N F E A L Q D F F R L F P E Y K N N K L F L T G E S
151 Y A G I Y I P T L A V L V M Q D P S M N L Q G L A V G N G L
181 S S Y E Q N D N S L V Y F A Y Y H G L L G N R L W S S L Q T
211 H C C S Q N K C N F Y D N K D L E C V T N L Q E V A R I V G
241 N S G L N I Y N L Y A P C A G G V P S H F R Y E K D T V V V
271 Q D L G N I F T R L P L K R M W H O A L L R S G D K V R M D
301 P P C T N T T A A S T Y L N N P Y V R K A L N I P E Q L P Q
331 W D M C N F L V N L Q Y R R L Y R S M N S Q Y L K L L S S Q
361 K Y Q I L L Y N G D V D M A C N F M G D E W F V D S L N Q K
391 M E V Q R R P W L V K Y G D S G E Q I A G F V K E F S H I A
421 F L T I K G A G H M V P T D K P L A A F T M F S R F L N K Q
451 P Y                                                     452
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Figure 13

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```
  1   A P D Q D E I Q R L P G L A K Q P S F R Q Y S G Y L K S S G
 31   S K H L H Y W F V E S Q K D P E N S P V V L W L N G G P G C
 61   S S L D G L L T E H G P F L V Q P D G V T L E Y N P Y S W N
 91   L I A N V L Y L E S P A G V G F S Y S D D K F Y A T N D T E
121   V A Q S N F E A L Q D F F R L F P E Y K N N K L F L T G E S
151   Y A G I Y I P T L A V L V M Q D P S M N L Q G L A V G N G L
181   S S Y E Q N D N S L V Y F A Y Y H G L L G N R L W S S L Q T
211   H C C S Q N K C N F Y D N K D L E C V T N L Q E V A R I V G
241   N S G L N I Y N L Y A P C A G G V P S H F R Y E K D T V V V
271   Q D L G N I F T R L P L K R M D P P C T N T T A A S T Y L N
301   N P Y V R K A L N I P E Q L P Q W D M C N F L V N L Q Y R R
331   L Y R S M N S Q Y L K L L S S Q K Y Q I L L Y N G D V D M A
361   C N F M G D E W F V D S L N Q K M E V Q R R P W L V K Y G D
391   S G E Q I A G F V K E F S H I A F L T I K G A G H M V P T D
421   K P L A A F T M F S R F L N K Q P Y
                                                        438
```

Figure 14

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```
                                          cβ1              cβ2                 cβ3
HPP    APDQDEHQRL  PGLAKQPSPR  QNSGYLKSS-  GS-KHLHYWF  VHSQKHPENS  EVVLWLNGGP
CPW    ------HARL  PGQP-AVDFD  MHSGHITVDE  GAGRSLFYLL  QHAPEHAQPA  HLVLWLNGGP
CPY    ------KHKDP KILGIDPNVT  QHTGYLDVE-  DHDKHFFFWT  FHSRNHPAKD  EVILWLNGGP
MODEL  ------AAAA  AAAA-AAAFA  AYSGYIAAAE  GAGRSLFYLL  AEAAADAQAA  PLVLWLNGGP

        Cα1             cβ4        cβ5               cβ6          100
HPP    GCSSLD-GLL  THHGPFLVQH  DGVTLEYNPY  SWNLIANVLY  IDSHAGVGFS  ISDDKF--YA
CPW    GCSSVAYLAS  HHHGAFRVKP  RGAGLVIHHL  FHHKHANVLF  IDSHAGVGFS  YTHTSSDIYT
CPY    GCSSLT-GLP  HHHGPSSIGH  DLKPIG-NPY  SWHSHNTVIP  IDQHVNVGFS  YSGSSG----V
MODEL  GCSSVAYGAS  AELGAFRVAP  AGAGLALHEY  AWHAVANVLF  LDSPAGVGFS  YAAT---IYA

             Cα2             cβ7       130              cβ8
HPP    TNDTEVAQSN  PEHLQDFHRL  FHHY--HHHK  LPFHGESYAG  IDFHTLA--V  LVHQDPSHHI
CPW    SGDNRTAHDS  YAHLAHHFEH  FHHY--HYRD  FYHHGESYAG  HVHHELSQLV  HHSKNPVIHI
CPY    SNTVAAGKDV  YNFLELFHDQ  FPHHVNHGQD  FHLHGESYAG  HVHVPASEI  LSHKDRNHHI
MODEL  AGDAATAAAS  YAALAAHFEA  FPAY---KYRD FYIAGESYAG  AYVPALSQLV  AASAAPAANL

          cβ8             Hα1             200               Hα2
HPP    QGLAVGNGLS  SYEQHDNSLV  YFAYY-HGLL  --HGNRLWSS  LQTHCCSQNK  CNFYDNKDLE
CPW    KGFMVGNGLI  --DDYHDYVG  TFEFW--WHH  ----GIVSDDT YRRLKEACLH  DSFIHPSPA-
CPY    TSVLIGNGLT  --DPLTQYNY  YEPHAC-GEG  GEPSVLPSEE  CSAMEDSLER  CLGLIESCYD
MODEL  AGAAVGNGLA  --DAAADAVG  TFAFW--WA-  ----------  ----------  ------AAAA

                           Hα3                              Hβ1       Hβ2
HPP    ----------  ---HGVTHLQE VARIVGHSGL  NIYHLYAPCA  GGVPSHPRYE  KDTVVVQDLG
CPW    ----------  ---HQAATDV  ATAEQ---GNI DHYSLYTPVC  NITSSTGS--  ----------
CPY    SQSVWSCVPA  TIYHHHAQLA  PYQR------  ----------  ----------  ----------
MODEL  ----------  ---AAAAAAA  AAAA-----  ----------  ----------  ----------

                           Hα1        Hβ3        300             Cα4          Cα5
HPP    NIFTRLPLKR  MWHQALLRSG  DKVRMDPPPC- ------TNTTA AST-YLNNPY  VRKAL--NIP
CPW    ----------  ----------  ------YDPC- -------TER  YSTAYYNRRD  VQMALHANVT
CPY    TGRNVYDIR-  ----------  ---KDCE  GGNLCYPTLQ  DIDDYLNQDY  VKEAVG----  ----------
MODEL  ----------  ----------  ------YDPC- ------TAA  ASTAYY----  ----------

                           Cα6                          330   Cα7          cβ9
HPP    EQLP-QWDMH  NPLVHLQYRR  LY------RSM NSQYLHHLSS QKYHHLLYNG  HVHMACNFMG
CPW    GAMNYTWATH  SDTIHTHWHD  AP-----RSM  LPIYREHLAA  G-LHHWVFSG  DHHAVVPLTA
CPY    AEVD-HYESH  NFDIHRNF--  LFAGDWMKPY  HTAVTIHLN-  QDLRHLVYAG  DHHFICNWLG
MODEL  -----WATC  SDAIHAAHHD  AP------RSM LAAYAELIAA  G-LAIAAFSG  DTDAAAAAAA

          Cα8             cβ10        440             Cβ11       cβ12        Cα9
HPP    DEWFVDSH--  --NQKMEVQR  R-HHLVKYGD  SGEQIHGFVK  EFSHIAFLTI  KGAGHHVHTDK
CPW    TRYSIGAH--  ----GLPTTTS WYHH----YDD --QEVGGHSQ  VYKGLTLVSV  RGAGHHVELHR
CPY    NKAMTDVHPW  KYDEEPASQK  VRHHT---AS  ITDEVAGEVK  SYKHPTYLRV  FNGGHHVHFDV
MODEL  AAAAAAAL--  ----------S WYPH----YDD --QEVGGHSA AYAAAALVSV  RGAGHHVPLAR

          Cα10             490
HPP    HLHHFTMFSR  FLHKQPY---  ------
CPW    HRGHLVLFQY  FLQGKPMPGQ  TKHAT
CPY    HHNHLSMVNE  WIHGGFSL--  ------
MODEL  PAAALVLFAY  FLQGAPM---  ------
```

Figure 15

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Bootstrapping cycle

```
┌─────────────────────────┐
│   best available        │
│   model coordinates     │
└─────────────────────────┘
            │
            ▼
┌─────────────────────────┐
│  SigmaA weighted map    │
│  2m|Fo| – D|Fc|         │
└─────────────────────────┘
            │
            ▼
┌─────────────────────────┐
│  2–fold averaging       │
│  (RAVE/CCP4)            │
└─────────────────────────┘
            │
            ▼
┌───────────────────────────────┐
│  model expansion/rebuilding    │
│  in averaged map   (O)         │
└───────────────────────────────┘
        │        │            │
        ▼        ▼            ▼
            ┌──────────┐  ┌──────────┐
            │  update  │  │update NCS │
            │  mask    │  │operators  │
            │ (MAMA/O) │  │   (O)    │
            └──────────┘  └──────────┘
```

Figure 16
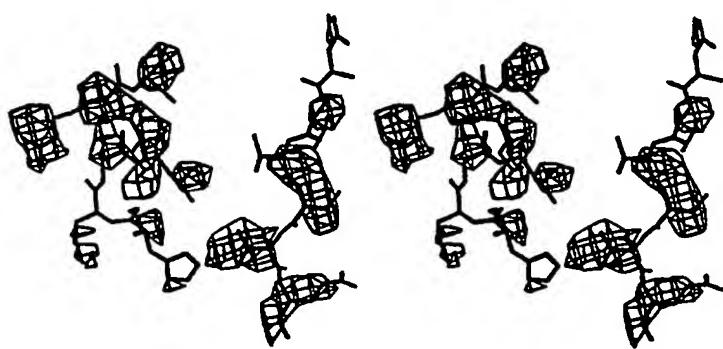
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Figure 17
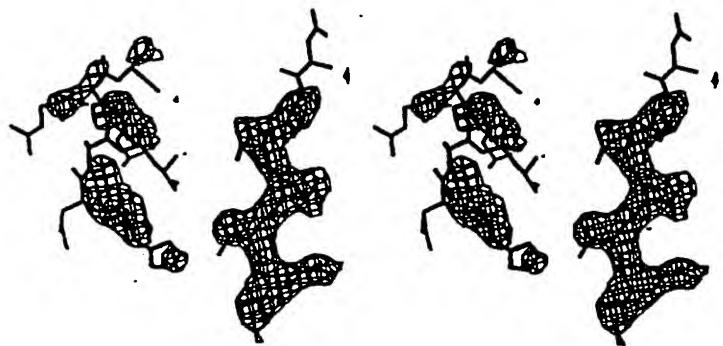
18/74
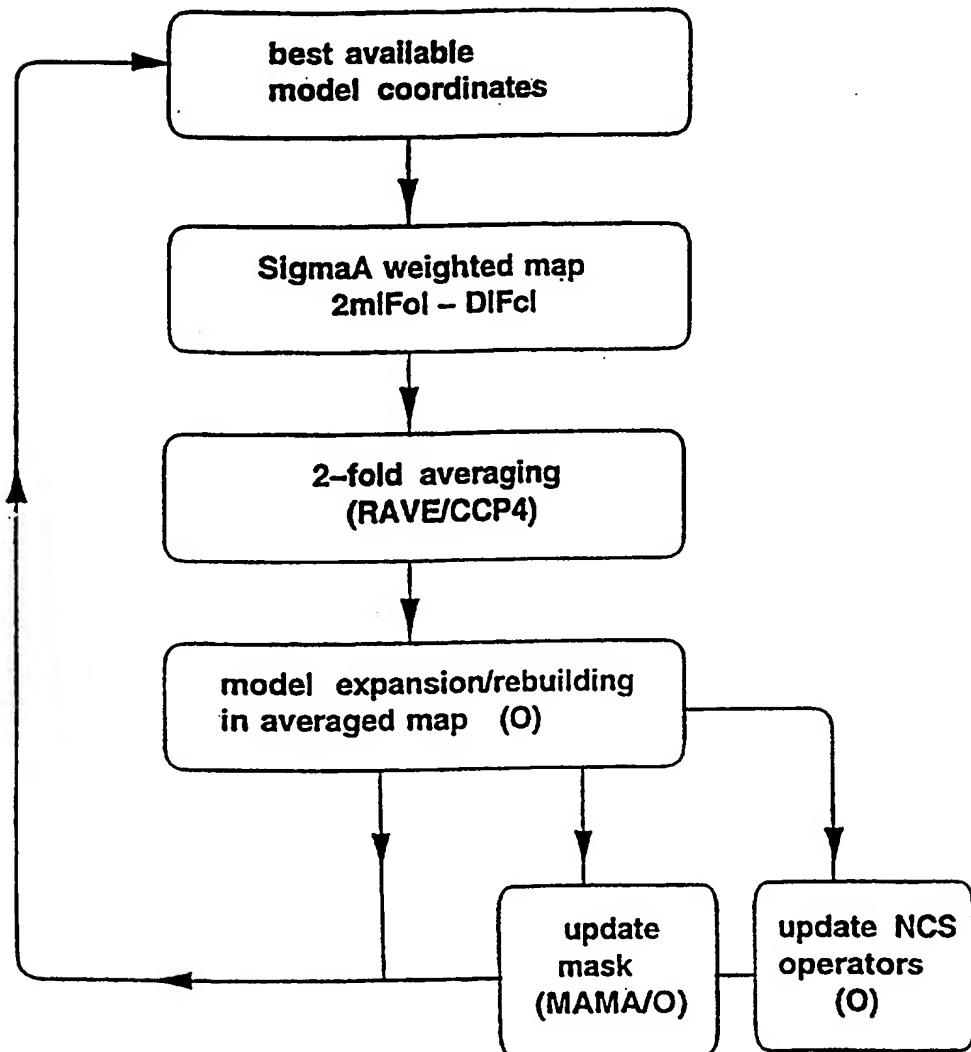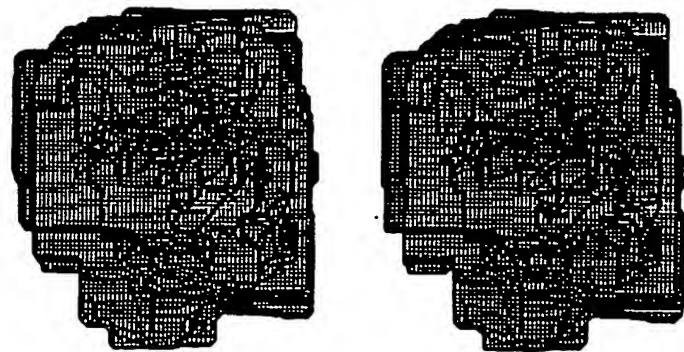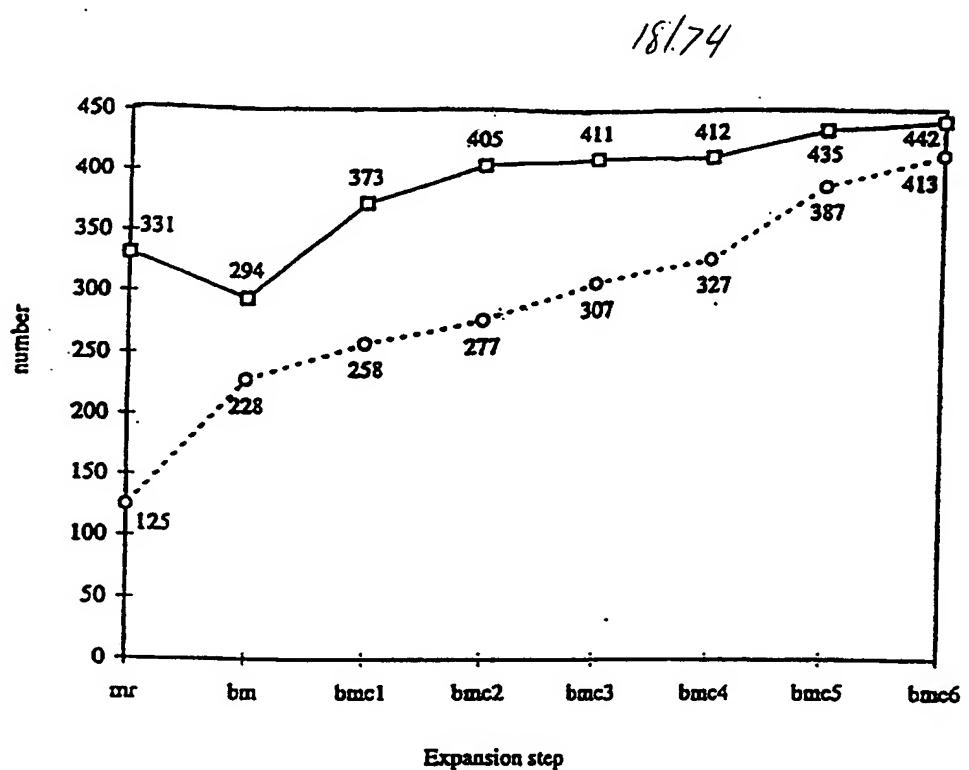
Figure 18

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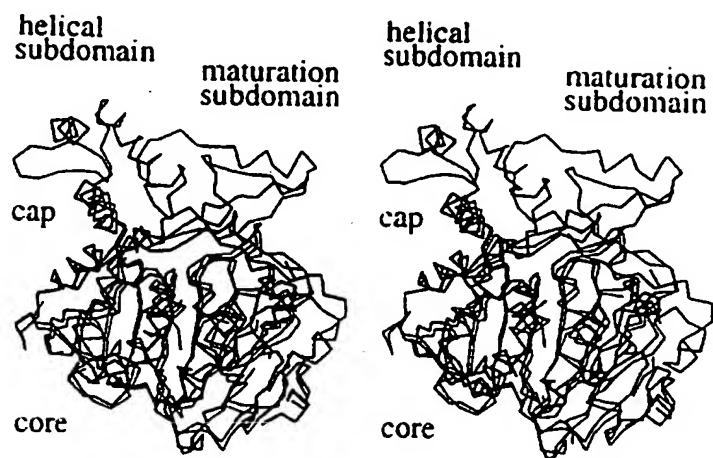
Figure 19
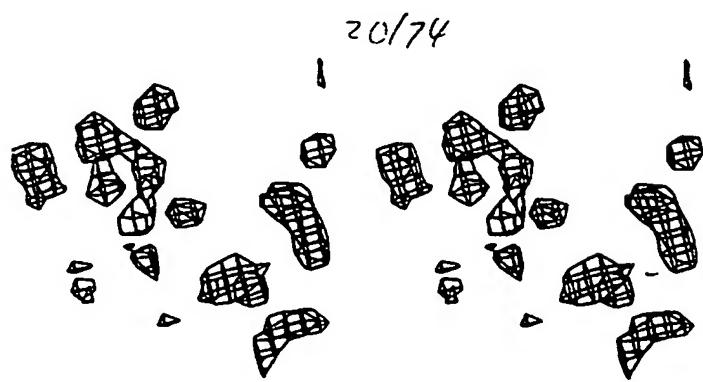
Figure 20A

Figure 20B

Figure 20C

Figure 20D

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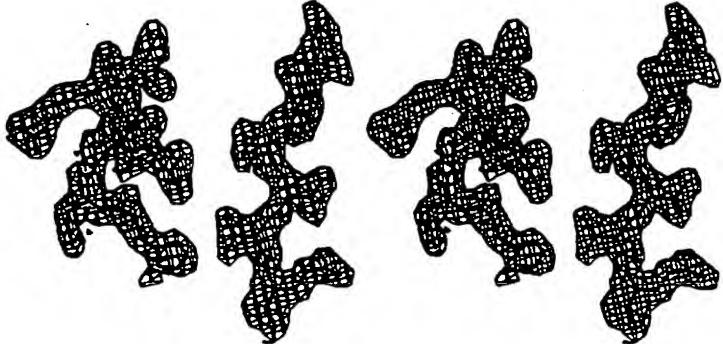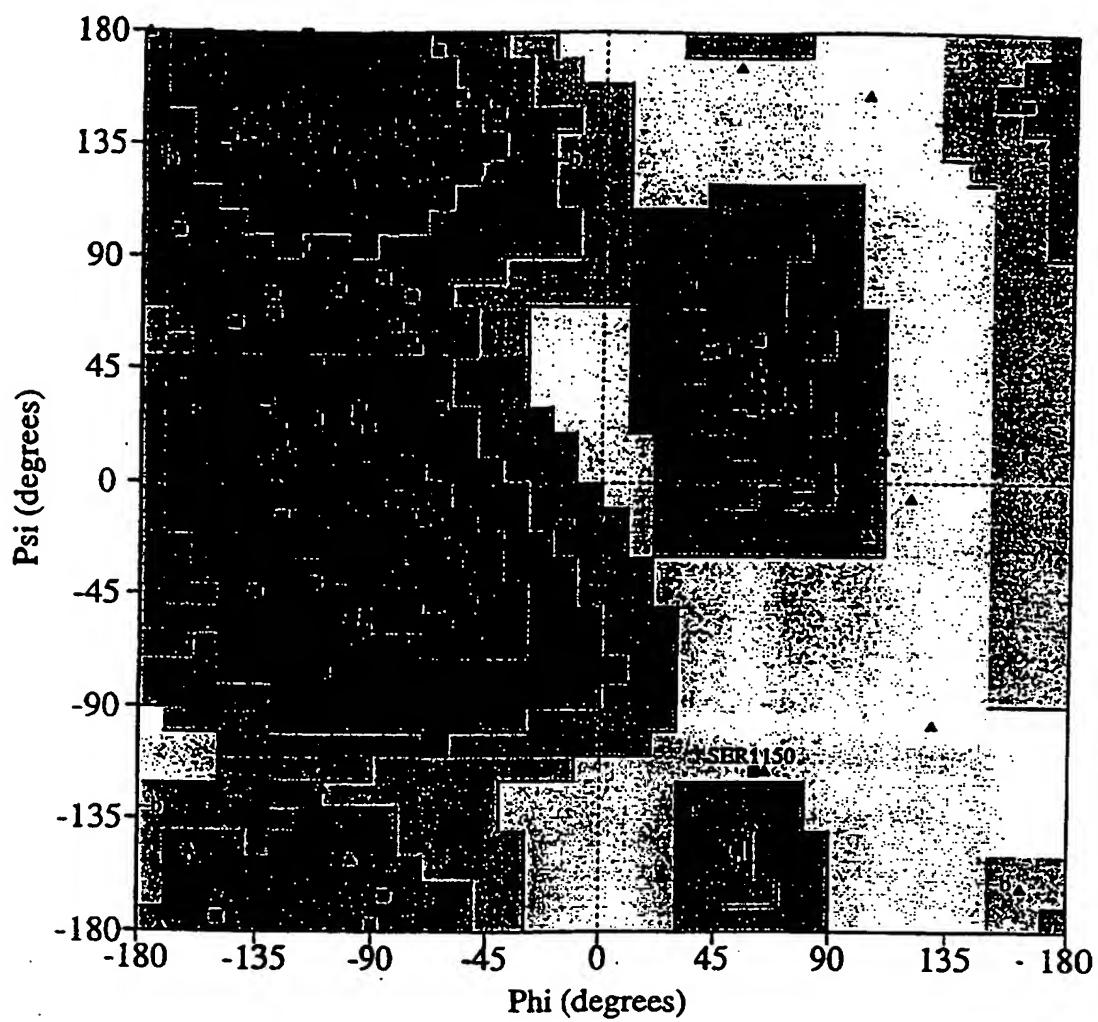
Figure 21

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COMPUTER SYSTEM 102

~104

CPU ~106

MAIN MEMORY ~108

CONTROL LOGIC

RAM

BUS

MONITOR ~120

SECONDARY MEMORY ~110

HARD DRIVE ~112

REMOVABLE STORAGE DEVICE

REMOVABLE STORAGE UNIT ~116

~114
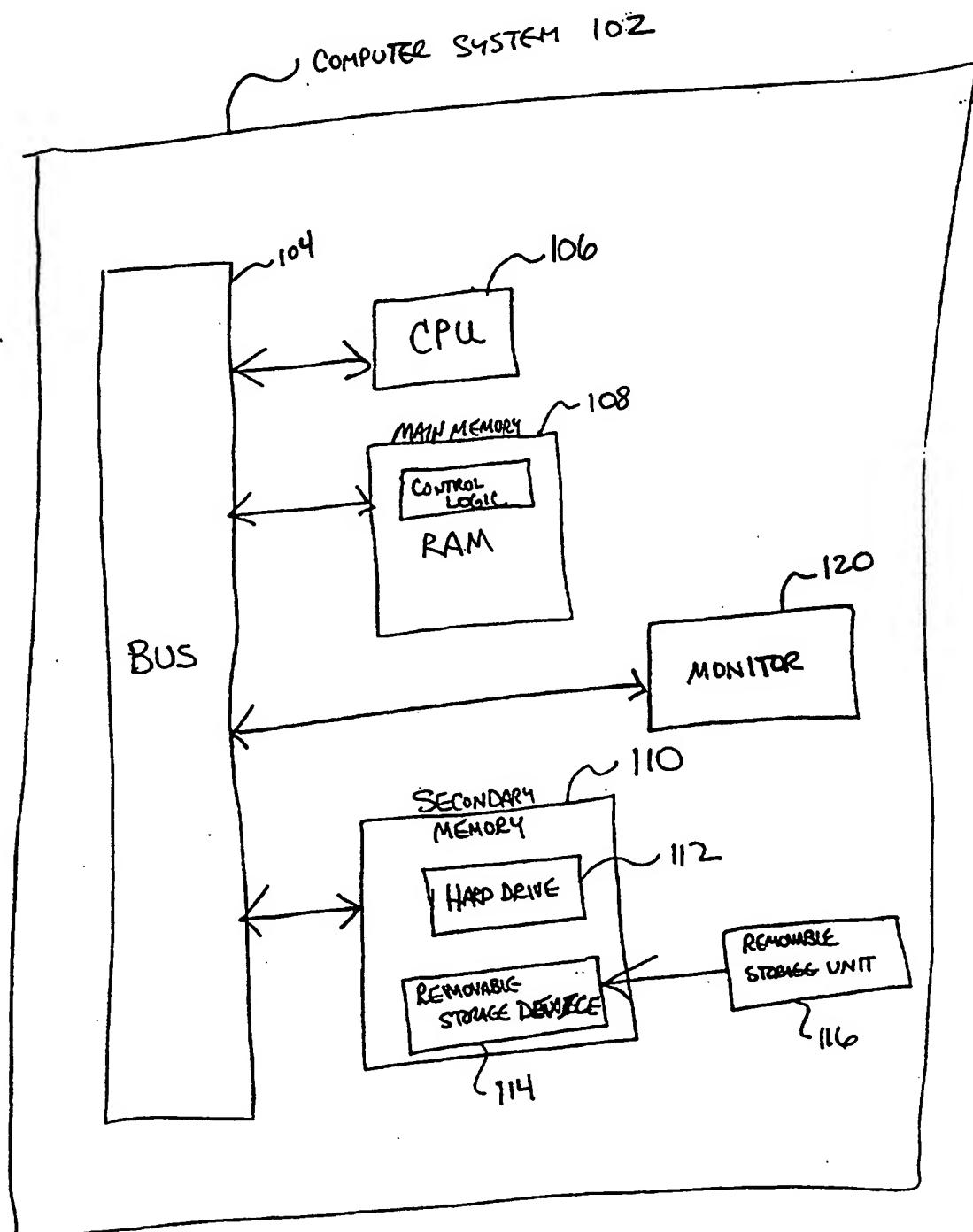
Figure 22

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```
CRYST1  115.040   148.110    80.970   90.00    90.00   90.00
ORIGX1        1.000000  0.000000  0.000000       0.00000
ORIGX2        0.000000  1.000000  0.000000     · 0.00000
ORIGX3        0.000000  0.000000  1.000000       0.00000
SCALE1        0.008693  0.000000  0.000000       0.00000
SCALE2        0.000000  0.006752  0.000000       0.00000
SCALE3        0.000000  0.000000  0.012350       0.00000
```

ATOM	397	N	VAL	50	36.021	62.379	-18.415	0.00	0.00	7
ATOM	398	CA	VAL	50	34.640	62.776	-18.328	0.00	0.00	6
ATOM	399	CB	VAL	50	34.127	63.418	-19.657	0.00	0.00	6
ATOM	400	CG1	VAL	50	32.623	63.580	-19.614	0.00	0.00	6
ATOM	401	CG2	VAL	50	34.774	64.795	-19.867	0.00	0.00	6
ATOM	402	C	VAL	50	33.952	61.433	-18.051	0.00	0.00	6
ATOM	403	O	VAL	50	34.283	60.412	-18.670	0.00	0.00	8
ATOM	404	N	VAL	51	33.060	61.424	-17.065	0.00	0.00	7
ATOM	405	CA	VAL	51	32.359	60.222	-16.675	0.00	0.00	6
ATOM	406	CB	VAL	51	32.821	59.761	-15.257	0.00	0.00	6
ATOM	407	CG1	VAL	51	31.931	58.602	-14.740	0.00	0.00	6
ATOM	408	CG2	VAL	51	34.290	59.373	-15.279	0.00	0.00	6
ATOM	409	C	VAL	51	30.872	60.478	-16.627	0.00	0.00	6
ATOM	410	O	VAL	51	30.415	61.272	-15.813	0.00	0.00	8
ATOM	411	N	LEU	52	30.117	59.815	-17.495	0.00	0.00	7
ATOM	412	CA	LEU	52	28.681	59.977	-17.479	0.00	0.00	6
ATOM	413	CB	LEU	52	28.082	59.634	-18.851	0.00	0.00	6
ATOM	414	CG	LEU	52	26.550	59.580	-18.920	0.00	0.00	6
ATOM	415	CD1	LEU	52	25.924	60.988	-18.820	0.00	0.00	6
ATOM	416	CD2	LEU	52	26.109	58.909	-20.219	0.00	0.00	6
ATOM	417	C	LEU	52	28.138	59.001	-16.441	0.00	0.00	6
ATOM	418	O	LEU	52	28.624	57.886	-16.346	0.00	0.00	8
ATOM	419	N	TRP	53	27.168	59.435	-15.647	0.00	0.00	7
ATOM	420	CA	TRP	53	26.546	58.567	-14.684	0.00	0.00	6
ATOM	421	CB	TRP	53	26.859	58.963	-13.230	0.00	0.00	6
ATOM	422	CG	TRP	53	26.038	58.120	-12.241	0.00	0.00	6
ATOM	423	CD2	TRP	53	26.338	56.786	-11.787	0.00	0.00	6
ATOM	424	CE2	TRP	53	25.273	56.374	-10.949	0.00	0.00	6
ATOM	425	CE3	TRP	53	27.407	55.903	-12.007	0.00	0.00	6
ATOM	426	CD1	TRP	53	24.834	58.443	-11.682	0.00	0.00	6
ATOM	427	NE1	TRP	53	24.370	57.399	-10.903	0.00	0.00	7
ATOM	428	CZ2	TRP	53	25.244	55.114	-10.326	0.00	0.00	6
ATOM	429	C23	TRP	53	27.380	54.644	-11.392	0.00	0.00	6
ATOM	430	CH2	TRP	53	26.306	54.266	-10.559	0.00	0.00	6
ATOM	431	C	TRP	53	25.046	58.570	-14.920	0.00	0.00	6
ATOM	432	O	TRP	53	24.413	59.626	-14.979	0.00	0.00	8
ATOM	433	N	LEU	54	24.479	57.387	-15.115	0.00	0.00	7
ATOM	434	CA	LEU	54	23.041	57.273	-15.306	0.00	0.00	6
ATOM	435	CB	LEU	54	22.708	56.740	-16.702	0.00	0.00	6
ATOM	436	CG	LEU	54	23.032	57.566	-17.936	0.00	0.00	6
ATOM	437	CD1	LEU	54	22.685	56.668	-19.137	0.00	0.00	6
ATOM	438	CD2	LEU	54	22.223	58.891	-17.958	0.00	0.00	6
ATOM	439	C	LEU	54	22.486	56.281	-14.317	0.00	0.00	6
ATOM	440	O	LEU	54	23.071	55.226	-14.108	0.00	0.00	8
ATOM	441	N	ASN	55	21.351	56.608	-13.726	0.00	0.00	7
ATOM	442	CA	ASN	55	20.688	55.725	-12.793	0.00	0.00	6
ATOM	443	CB	ASN	55	20.032	56.536	-11.652	0.00	0.00	6
ATOM	444	CG	ASN	55	20.936	56.660	-10.429	0.00	0.00	6
ATOM	445	OD1	ASN	55	21.657	57.646	-10.237	0.00	0.00	8
ATOM	446	ND2	ASN	55	20.933	55.631	-9.616	0.00	0.00	7
ATOM	447	C	ASN	55	19.664	54.990	-13.661	0.00	0.00	6
ATOM	448	O	ASN	55	19.648	55.169	-14.877	0.00	0.00	8

Figure 23.1

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ATOM	449	N	GLY	56	18.785	54.195	-13.073	0.00	0.00	7
ATOM	450	CA	GLY	56	17.852	53.473	-13.910	0.00	0.00	6
ATOM	451	C	GLY	56	16.396	53.736	-13.709	0.00	0.00	6
ATOM	452	O	GLY	56	15.913	54.855	-13.903	0.00	0.00	8
ATOM	453	N	GLY	57	15.677	52.655	-13.421	0.00	0.00	7
ATOM	454	CA	GLY	57	14.251	52.709	-13.205	0.00	0.00	6
ATOM	455	C	GLY	57	13.593	51.518	-13.880	0.00	0.00	6
ATOM	456	O	GLY	57	13.493	50.460	-13.247	0.00	0.00	8
ATOM	457	N	PRO	58	13.172	51.628	-15.166	0.00	0.00	7
ATOM	458	CD	PRO	58	12.540	50.553	-15.962	0.00	0.00	6
ATOM	459	CA	PRO	58	13.304	52.837	-15.985	0.00	0.00	6
ATOM	460	CB	PRO	58	12.968	52.332	-17.402	0.00	0.00	6
ATOM	461	CG	PRO	58	11.954	51.304	-17.155	0.00	0.00	6
ATOM	462	C	PRO	58	12.358	53.953	-15.536	0.00	0.00	6
ATOM	463	O	PRO	58	11.229	53.697	-15.113	0.00	0.00	8
ATOM	464	N	GLY	59	12.868	55.178	-15.559	0.00	0.00	7
ATOM	465	CA	GLY	59	12.066	56.326	-15.176	0.00	0.00	6
ATOM	466	C	GLY	59	12.517	57.033	-13.914	0.00	0.00	6
ATOM	467	O	GLY	59	11.765	57.840	-13.410	0.00	0.00	8
ATOM	468	N	CYS	60	13.714	56.724	-13.416	0.00	0.00	7
ATOM	469	CA	CYS	60	14.250	57.331	-12.192	0.00	0.00	6
ATOM	470	C	CYS	60	15.438	58.284	-12.465	0.00	0.00	6
ATOM	471	O	CYS	60	16.164	58.149	-13.469	0.00	0.00	8
ATOM	472	CB	CYS	60	14.622	56.255	-11.136	0.00	0.00	6
ATOM	473	SG	CYS	60	13.226	55.179	-10.628	0.00	0.00	16
ATOM	474	N	SER	61	15.643	59.211	-11.535	0.00	0.00	7
ATOM	475	CA	SER	61	16.652	60.256	-11.628	0.00	0.00	6
ATOM	476	CB	SER	61	16.133	61.457	-10.818	0.00	0.00	6
ATOM	477	OG	SER	61	17.135	62.428	-10.630	0.00	0.00	8
ATOM	478	C	SER	61	18.109	59.946	-11.244	0.00	0.00	6
ATOM	479	O	SER	61	18.358	59.345	-10.207	0.00	0.00	8
ATOM	480	N	SER	62	19.057	60.441	-12.058	0.00	0.00	7
ATOM	481	CA	SER	62	20.508	60.290	-11.849	0.00	0.00	6
ATOM	482	CB	SER	62	21.302	60.634	-13.126	0.00	0.00	6
ATOM	483	OG	SER	62	21.116	59.682	-14.165	0.00	0.00	8
ATOM	484	C	SER	62	21.016	61.181	-10.719	0.00	0.00	6
ATOM	485	O	SER	62	22.177	61.100	-10.319	0.00	0.00	8
ATOM	486	N	LEU	63	20.160	62.088	-10.259	0.00	0.00	7
ATOM	487	CA	LEU	63	20.508	62.981	-9.148	0.00	0.00	6
ATOM	488	CB	LEU	63	19.515	64.138	-9.053	0.00	0.00	6
ATOM	489	CG	LEU	63	19.576	64.997	-10.303	0.00	0.00	6
ATOM	490	CD1	LEU	63	18.999	66.339	-9.936	0.00	0.00	6
ATOM	491	CD2	LEU	63	21.005	65.110	-10.828	0.00	0.00	6
ATOM	492	C	LEU	63	20.515	62.163	-7.861	0.00	0.00	6
ATOM	493	O	LEU	63	21.000	62.605	-6.819	0.00	0:00	8
ATOM	494	N	ASP	64	19.916	60.984	-7.956	0.00	0.00	7
ATOM	495	CA	ASP	64	19.874	60.008	-6.885	0.00	0.00	6
ATOM	496	CB	ASP	64	19.012	58.838	-7.335	0.00	0.00	6
ATOM	497	CG	ASP	64	18.860	57.759	-6.291	0.00	0.00	6
ATOM	498	OD1	ASP	64	19.314	57.931	-5.132	0.00	0.00	8
ATOM	499	OD2	ASP	64	18.255	56.723	-6.643	0.00	0.00	8
ATOM	500	C	ASP	64	21.332	59.592	-6.749	0.00	0.00	6
ATOM	501	O	ASP	64	21.886	59.648	-5.668	0.00	0.00	8
ATOM	502	N	GLY	65	21.992	59.287	-7.864	0.00	0.00	7
ATOM	503	CA	GLY	65	23.390	58.909	-7.792	0.00	0.00	6
ATOM	504	C	GLY	65	24.241	60.018	-7.200	0.00	0.00	6
ATOM	505	O	GLY	65	25.236	59.761	-6.526	0.00	0.00	8
ATOM	506	N	LEU	66	23.856	61.262	-7.446	0.00	0.00	7
ATOM	507	CA	LEU	66	24.602	62.427	-6.952	0.00	0.00	6
ATOM	508	CB	LEU	66	24.219	63.715	-7.736	0.00	0.00	6

Figure 23.2

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ATOM	509	CG	LEU	66	25.197	64.918	-7.715	0.00	0.00	6
ATOM	510	CD1	LEU	66	24.924	65.836	-8.873	0.00	0.00	6
ATOM	511	CD2	LEU	66	25.137	65.700	-6.413	0.00	0.00	6
ATOM	512	C	LEU	66	24.384	62.665	-5.478	0.00	0.00	6
ATOM	513	O	LEU	66	25.300	62.541	-4.674	0.00	0.00	8
ATOM	514	N	LEU	67	23.151	63.002	-5.153	0.00	0.00	7
ATOM	515	CA	LEU	67	22.754	63.315	-3.792	0.00	0.00	6
ATOM	516	CB	LEU	67	21.392	64.015	-3.812	0.00	0.00	6
ATOM	517	CG	LEU	67	21.406	65.358	-4.557	0.00	0.00	6
ATOM	518	CD1	LEU	67	20.026	65.954	-4.615	0.00	0.00	6
ATOM	519	CD2	LEU	67	22.351	66.311	-3.868	0.00	0.00	6
ATOM	520	C	LEU	67	22.764	62.177	-2.773	0.00	0.00	6
ATOM	521	O	LEU	57	22.826	62.446	-1.578	0.00	0.00	8
ATOM	522	N	THR	68	22.653	60.923	-3.209	0.00	0.00	7
ATOM	523	CA	THR	68	22.644	59.833	-2.248	0.00	0.00	6
ATOM	524	CB	THR	68	21.271	59.151	-2.150	0.00	0.00	6
ATOM	525	OG1	THR	68	21.197	58.063	-3.080	0.00	0.00	8
ATOM	526	CG2	THR	68	20.141	60.138	-2.433	0.00	0.00	6
ATOM	527	C	THR	68	23.694	58.746	-2.407	0.00	0.00	6
ATOM	528	O	THR	68	23.931	57.988	-1.463	0.00	0.00	8
ATOM	529	N	GLU	69	24.357	58.707	-3.566	0.00	0.00	7
ATOM	530	CA	GLU	69	25.376	57.694	-3.853	0.00	0.00	6
ATOM	531	CB	GLU	69	25.062	56.954	-5.156	0.00	0.00	6
ATOM	532	CG	GLU	69	23.739	56.278	-5.130	0.00	0.00	6
ATOM	533	CD	GLU	69	23.517	55.370	-6.308	0.00	0.00	6
ATOM	534	OE1	GLU	69	24.108	54.278	-6.317	0.00	0.00	8
ATOM	535	OE2	GLU	69	22.731	55.733	-7.214	0.00	0.00	8
ATOM	536	C	GLU	69	26.822	58.134	-3.859	0.00	0.00	6
ATOM	537	O	GLU	69	27.568	57.843	-2.920	0.00	0.00	8
ATOM	538	N	HIS	70	27.262	58.812	-4.905	0.00	0.00	7
ATOM	539	CA	HIS	70	28.658	59.215	-4.953	0.00	0.00	6
ATOM	540	CB	HIS	70	29.455	58.238	-5.816	0.00	0.00	6
ATOM	541	CG	HIS	70	28.876	58.067	-7.185	0.00	0.00	6
ATOM	542	CD2	HIS	70	28.346	58.969	-8.044	0.00	0.00	6
ATOM	543	ND1	HIS	70	28.747	56.832	-7.792	0.00	0.00	7
ATOM	544	CE1	HIS	70	28.147	56.986	-8.960	0.00	0.00	6
ATOM	545	NE2	HIS	70	27.894	58.272	-9.135	0.00	0.00	7
ATOM	546	C	HIS	70	28.927	60.640	-5.424	0.00	0.00	6
ATOM	547	O	HIS	70	29.979	60.890	-6.024	0.00	0.00	8
ATOM	548	N	GLY	71	27.965	61.535	-5.192	0.00	0.00	7
ATOM	549	CA	GLY	71	28.122	62.937	-5.556	0.00	0.00	6
ATOM	550	C	GLY	71	29.095	63.607	-4.605	0.00	0.00	6
ATOM	551	O	GLY	71	29.423	63.023	-3.560	0.00	0.00	8
ATOM	552	N	PRO	72	29.589	64.815	-4.916	0.00	0.00	7
ATOM	553	CD	PRO	72	29.328	65.626	-6.110	0.00	0.00	6
ATOM	554	CA	PRO	72	30.543	65.490	-4.024	0.00	0.00	6
ATOM	555	CB	PRO	72	30.948	66.730	-4.831	0.00	0.00	6
ATOM	556	CG	PRO	72	29.757	66.995	-5.670	0.00	0.00	6
ATOM	557	C	PRO	72	30.011	65.832	-2.627	0.00	0.00	6
ATOM	558	O	PRO	72	30.783	66.042	-1.695	0.00	0.00	8
ATOM	559	N	PHE	73	28.695	65.802	-2.489	0.00	0.00	7
ATOM	560	CA	PHE	73	28.012	66.098	-1.245	0.00	0.00	6
ATOM	561	CB	PHE	73	27.743	67.609	-1.119	0.00	0.00	6
ATOM	562	CG	PHE	73	27.575	68.324	-2.448	0.00	0.00	6
ATOM	563	CD1	PHE	73	26.419	68.168	-3.212	0.00	0.00	6
ATOM	564	CD2	PHE	73	28.590	69.142	-2.940	0.00	0.00	6
ATOM	565	CE1	PHE	73	26.284	68.814	-4.435	0.00	0.00	6
ATOM	566	CE2	PHE	73	28.453	69.787	-4.167	0.00	0.00	6
ATOM	567	CZ	PHE	73	27.307	69.621	-4.908	0.00	0.00	6
ATOM	568	C	PHE	73	26.721	65.310	-1.303	0.00	0.00	6

Figure 23.3

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ATOM   569  O    PHE   73    26.197  65.073  -2.388  0.00  0.00   8
ATOM   570  N    LEU   74    26.190  64.931  -0.149  0.00  0.00   7
ATOM   571  CA   LEU   74    24.988  64.116  -0.099  0.00  0.00   6
ATOM   572  CB   LEU   74    25.321  62.723   0.458  0.00  0.00   6
ATOM   573  CG   LEU   74    26.519  61.983  -0.157  0.00  0.00   6
ATOM   574  CD1  LEU   74    26.931  60.816   0.738  0.00  0.00   6
ATOM   575  CD2  LEU   74    26.187  61.499  -1.577  0.00  0.00   6
ATOM   576  C    LEU   74    23.986  64.772   0.769  0.00  0.00   6
ATOM   577  O    LEU   74    24.339  65.469   1.696  0.00  0.00   8
ATOM   578  N    VAL   75    22.724  64.521   0.486  0.00  0.00   7
ATOM   579  CA   VAL   75    21.650  65.118   1.227  0.00  0.00   6
ATOM   580  CB   VAL   75    20.342  65.185   0.360  0.00  0.00   6
ATOM   581  CG1  VAL   75    19.715  63.790   0.159  0.00  0.00   6
ATOM   582  CG2  VAL   75    19.369  66.187   0.936  0.00  0.00   6
ATOM   583  C    VAL   75    21.450  64.417   2.558  0.00  0.00   6
ATOM   584  O    VAL   75    21.570  63.194   2.660  0.00  0.00   8
ATOM   585  N    GLN   76    21.231  65.225   3.587  0.00  0.00   7
ATOM   586  CA   GLN   76    21.027  64.740   4.934  0.00  0.00   6
ATOM   587  CB   GLN   76    21.641  65.720   5.926  0.00  0.00   6
ATOM   588  CG   GLN   76    23.111  65.961   5.650  0.00  0.00   6
ATOM   589  CD   GLN   76    23.908  64.661   5.616  0.00  0.00   6
ATOM   590  OE1  GLN   76    23.813  63.856   6.530  0.00  0.00   8
ATOM   591  NE2  GLN   76    24.673  64.450   4.558  0.00  0.00   7
ATOM   592  C    GLN   76    19.544  64.575   5.137  0.00  0.00   6
ATOM   593  O    GLN   76    18.735  65.178   4.421  0.00  0.00   8
=================================================================
ATOM  1143  N    LEU  144    36.448  59.438 -22.280  0.00  0.00   7
ATOM  1144  CA   LEU  144    35.062  59.374 -21.895  0.00  0.00   6
ATOM  1145  CB   LEU  144    34.163  59.717 -23.088  0.00  0.00   6
ATOM  1146  CG   LEU  144    32.662  59.606 -22.853  0.00  0.00   6
ATOM  1147  CD1  LEU  144    32.187  60.673 -21.879  0.00  0.00   6
ATOM  1148  CD2  LEU  144    31.906  59.698 -24.195  0.00  0.00   6
ATOM  1149  C    LEU  144    34.765  57.972 -21.343  0.00  0.00   6
ATOM  1150  O    LEU  144    35.265  56.966 -21.854  0.00  0.00   8
ATOM  1151  N    PHE  145    34.003  57.937 -20.255  0.00  0.00   7
ATOM  1152  CA   PHE  145    33.601  56.700 -19.601  0.00  0.00   6
ATOM  1153  CB   PHE  145    34.297  56.550 -18.229  0.00  0.00   6
ATOM  1154  CG   PHE  145    35.746  56.139 -18.335  0.00  0.00   6
ATOM  1155  CD1  PHE  145    36.760  57.091 -18.338  0.00  0.00   6
ATOM  1156  CD2  PHE  145    36.099  54.794 -18.458  0.00  0.00   6
ATOM  1157  CE1  PHE  145    38.104  56.714 -18.465  0.00  0.00   6
ATOM  1158  CE2  PHE  145    37.438  54.408 -18.581  0.00  0.00   6
ATOM  1159  CZ   PHE  145    38.440  55.379 -18.585  0.00  0.00   6
ATOM  1160  C    PHE  145    32.115  56.802 -19.408  0.00  0.00   6
ATOM  1161  O    PHE  145    31.617  57.883 -19.092  0.00  0.00   8
ATOM  1162  N    LEU  146    31.397  55.724 -19.713  0.00  0.00   7
ATOM  1163  CA   LEU  146    29.943  55.687 -19.533  0.00  0.00   6
ATOM  1164  CB   LEU  146    29.262  55.231 -20.828  0.00  0.00   6
ATOM  1165  CG   LEU  146    29.623  56.058 -22.074  0.00  0.00   6
ATOM  1166  CD1  LEU  146    29.081  55.334 -23.292  0.00  0.00   6
ATOM  1167  CD2  LEU  146    29.072  57.489 -21.979  0.00  0.00   6
ATOM  1168  C    LEU  146    29.621  54.726 -18.362  0.00  0.00   6
ATOM  1169  O    LEU  146    29.873  53.517 -18.447  0.00  0.00   8
ATOM  1170  N    THR  147    29.055  55.256 -17.278  0.00  0.00   7
ATOM  1171  CA   THR  147    28.776  54.433 -16.105  0.00  0.00   6
ATOM  1172  CB   THR  147    29.745  54.778 -14.961  0.00  0.00   6
ATOM  1173  OG1  THR  147    29.460  56.099 -14.501  0.00  0.00   8
ATOM  1174  CG2  THR  147    31.212  54.724 -15.432  0.00  0.00   6
ATOM  1175  C    THR  147    27.339  54.610 -15.650  0.00  0.00   6
ATOM  1176  O    THR  147    26.719  55.634 -15.900  0.00  0.00   8
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Figure 23.4

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ATOM	1177	N	GLY	148	26.788	53.592	-15.001	0.00	0.00	7
ATOM	1178	CA	GLY	148	25.409	53.688	-14.585	0.00	0.00	6
ATOM	1179	C	GLY	148	25.084	52.506	-13.709	0.00	0.00	6
ATOM	1180	O	GLY	148	25.942	51.643	-13.479	0.00	0.00	8
ATOM	1181	N	GLU	149	23.824	52.380	-13.316	0.00	0.00	7
ATOM	1182	CA	GLU	149	23.468	51.306	-12.416	0.00	0.00	6
ATOM	1183	CB	GLU	149	23.665	51.853	-10.986	0.00	0.00	6
ATOM	1184	CG	GLU	149	22.835	51.240	-9.877	0.00	0.00	6
ATOM	1185	CD	GLU	149	22.897	52.051	-8.596	0.00	0.00	6
ATOM	1186	OE1	GLU	149	21.834	52.483	-8.131	0.00	0.00	8
ATOM	1187	OE2	GLU	149	23.999	52.251	-8.057	0.00	0.00	8
ATOM	1188	C	GLU	149	22.043	50.843	-12.622	0.00	0.00	6
ATOM	1189	O	GLU	149	21.222	51.572	-13.185	0.00	0.00	8
ATOM	1190	N	SER	150	21.767	49.592	-12.278	0.00	0.00	7
ATOM	1191	CA	SER	150	20.400	49.105	-12.366	0.00	0.00	6
ATOM	1192	CB	SER	150	19.522	50.063	-11.538	0.00	0.00	6
ATOM	1193	OG	SER	150	18.222	49.539	-11.251	0.00	0.00	8
ATOM	1194	C	SER	150	19.904	48.980	-13.825	0.00	0.00	6
ATOM	1195	O	SER	150	20.505	48.270	-14.622	0.00	0.00	8
ATOM	1196	N	TYR	151	18.822	49.675	-14.177	0.00	0.00	7
ATOM	1197	CA	TYR	151	18.302	49.623	-15.533	0.00	0.00	6
ATOM	1198	CB	TYR	151	16.965	50.337	-15.675	0.00	0.00	6
ATOM	1199	CG	TYR	151	16.241	49.935	-16.945	0.00	0.00	6
ATOM	1200	CD1	TYR	151	15.527	48.751	-16.995	0.00	0.00	6
ATOM	1201	CE1	TYR	151	14.953	48.306	-18.157	0.00	0.00	6
ATOM	1202	CD2	TYR	151	16.356	50.679	-18.115	0.00	0.00	6
ATOM	1203	CE2	TYR	151	15.788	50.242	-19.290	0.00	0.00	6
ATOM	1204	CZ	TYR	151	15.089	49.047	-19.298	0.00	0.00	6
ATOM	1205	OH	TYR	151	14.497	48.570	-20.435	0.00	0.00	8
ATOM	1206	C	TYR	151	19.315	50.228	-16.485	0.00	0.00	6
ATOM	1207	O	TYR	151	19.260	49.965	-17.683	0.00	0.00	8
ATOM	1208	N	ALA	152	20.259	51.018	-15.965	0.00	0.00	7
ATOM	1209	CA	ALA	152	21.288	51.581	-16.813	0.00	0.00	6
ATOM	1210	CB	ALA	152	22.089	52.610	-16.082	0.00	0.00	6
ATOM	1211	C	ALA	152	22.186	50.433	-17.271	0.00	0.00	6
ATOM	1212	O	ALA	152	23.256	50.657	-17.804	0.00	0.00	8
ATOM	1213	N	GLY	153	21.796	49.198	-16.961	0.00	0.00	7
ATOM	1214	CA	GLY	153	22.536	48.043	-17.429	0.00	0.00	6
ATOM	1215	C	GLY	153	22.133	47.843	-18.889	0.00	0.00	6
ATOM	1216	O	GLY	153	22.790	47.120	-19.639	0.00	0.00	8
ATOM	1217	N	ILE	154	20.980	48.407	-19.249	0.00	0.00	7
ATOM	1218	CA	ILE	154	20.462	48.384	-20.627	0.00	0.00	6
ATOM	1219	CB	ILE	154	18.911	48.220	-20.665	0.00	0.00	6
ATOM	1220	CG2	ILE	154	18.394	48.228	-22.129	0.00	0.00	6
ATOM	1221	CG1	ILE	154	18.441	46.989	-19.861	0.00	0.00	6
ATOM	1222	CD1	ILE	154	18.441	45.716	-20.587	0.00	0.00	6
ATOM	1223	C	ILE	154	20.845	49.759	-21.247	0.00	0.00	6
ATOM	1224	O	ILE	154	21.425	49.819	-22.324	0.00	0.00	8
ATOM	1225	N	TYR	155	20.578	50.854	-20.535	0.00	0.00	7
ATOM	1226	CA	TYR	155	20.918	52.193	-21.022	0.00	0.00	6
ATOM	1227	CB	TYR	155	20.694	53.278	-19.950	0.00	0.00	6
ATOM	1228	CG	TYR	155	19.300	53.539	-19.449	0.00	0.00	6
ATOM	1229	CD1	TYR	155	19.117	54.164	-18.226	0.00	0.00	6
ATOM	1230	CE1	TYR	155	17.846	54.508	-17.779	0.00	0.00	6
ATOM	1231	CD2	TYR	155	18.179	53.252	-20.210	0.00	0.00	6
ATOM	1232	CE2	TYR	155	16.912	53.579	-19.775	0.00	0.00	6
ATOM	1233	CZ	TYR	155	16.752	54.215	-18.558	0.00	0.00	6
ATOM	1234	OH	TYR	155	15.510	54.595	-18.114	0.00	0.00	8
ATOM	1235	C	TYR	155	22.378	52.340	-21.436	0.00	0.00	6
ATOM	1236	O	TYR	155	22.691	52.886	-22.497	0.00	0.00	8

Figure 23.5

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ATOM	1365	N	GLY	173	35.881	53.475	-21.853	0.00	0.00	7
ATOM	1366	CA	GLY	173	35.360	52.368	-21.082	0.00	0.00	6
ATOM	1367	C	GLY	173	33.978	52.596	-20.551	0.00	0.00	6
ATOM	1368	O	GLY	173	33.420	53.674	-20.690	0.00	0.00	8
ATOM	1369	N	LEU	174	33.401	51.545	-19.983	0.00	0.00	7
ATOM	1370	CA	LEU	174	32.074	51.619	-19.384	0.00	0.00	6
ATOM	1371	CB	LEU	174	30.977	51.192	-20.377	0.00	0.00	6
ATOM	1372	CG	LEU	174	31.094	49.922	-21.229	0.00	0.00	6
ATOM	1373	CD1	LEU	174	29.715	49.504	-21.640	0.00	0.00	6
ATOM	1374	CD2	LEU	174	31.989	50.148	-22.413	0.00	0.00	6
ATOM	1375	C	LEU	174	32.045	50.765	-18.112	0.00	0.00	6
ATOM	1376	O	LEU	174	32.846	49.837	-17.967	0.00	0.00	8
ATOM	1377	N	ALA	175	31.182	51.131	-17.172	0.00	0.00	7
ATOM	1378	CA	ALA	175	31.060	50.408	-15.914	0.00	0.00	6
ATOM	1379	CB	ALA	175	31.896	51.072	-14.833	0.00	0.00	6
ATOM	1380	C	ALA	175	29.615	50.378	-15.510	0.00	0.00	6
ATOM	1381	O	ALA	175	28.936	51.408	-15.528	0.00	0.00	8
ATOM	1382	N	VAL	176	29.130	49.187	-15.171	0.00	0.00	7
ATOM	1383	CA	VAL	176	27.736	49.007	-14.783	0.00	0.00	6
ATOM	1384	CB	VAL	176	26.985	48.172	-15.858	0.00	0.00	6
ATOM	1385	CG1	VAL	176	25.619	47.729	-15.337	0.00	0.00	6
ATOM	1386	CG2	VAL	176	26.802	49.018	-17.145	0.00	0.00	6
ATOM	1387	C	VAL	176	27.608	48.356	-13.402	0.00	0.00	6
ATOM	1388	O	VAL	176	28.162	47.268	-13.157	0.00	0.00	8
ATOM	1389	N	GLY	177	26.816	48.980	-12.533	0.00	0.00	7
ATOM	1390	CA	GLY	177	26.652	48.476	-11.187	0.00	0.00	6
ATOM	1391	C	GLY	177	25.308	47.860	-11.030	0.00	0.00	6
ATOM	1392	O	GLY	177	24.314	48.505	-11.369	0.00	0.00	8
ATOM	1393	N	ASN	178	25.263	46.625	-10.524	0.00	0.00	7
ATOM	1394	CA	ASN	178	23.996	45.890	-10.352	0.00	0.00	6
ATOM	1395	CB	ASN	178	23.302	46.250	-9.038	0.00	0.00	6
ATOM	1396	CG	ASN	178	24.002	45.646	-7.845	0.00	0.00	6
ATOM	1397	OD1	ASN	178	25.088	46.082	-7.486	0.00	0.00	8
ATOM	1398	ND2	ASN	178	23.470	44.542	-7.328	0.00	0.00	7
ATOM	1399	C	ASN	178	23.079	46.132	-11.520	0.00	0.00	6
ATOM	1400	O	ASN	178	21.897	46.472	-11.358	0.00	0.00	8
ATOM	1401	N	GLY	179	23.639	45.931	-12.708	0.00	0.00	7
ATOM	1402	CA	GLY	179	22.891	46.171	-13.923	0.00	0.00	6
ATOM	1403	C	GLY	179	22.028	45.045	-14.409	0.00	0.00	6
ATOM	1404	O	GLY	179	22.367	43.883	-14.231	0.00	0.00	8
ATOM	1405	N	LEU	180	20.913	45.399	-15.033	0.00	0.00	7
ATOM	1406	CA	LEU	180	19.988	44.434	-15.597	0.00	0.00	6
ATOM	1407	CB	LEU	180	18.578	45.029	-15.601	0.00	0.00	6
ATOM	1408	CG	LEU	180	17.450	44.240	-16.246	0.00	0.00	6
ATOM	1409	CD1	LEU	180	17.328	42.882	-15.581	0.00	0.00	6
ATOM	1410	CD2	LEU	180	16.156	45.021	-16.128	0.00	0.00	6
ATOM	1411	C	LEU	180	20.450	44.069	-17.025	0.00	0.00	6
ATOM	1412	O	LEU	180	19.909	44.564	-18.017	0.00	0.00	8
ATOM	1413	N	SER	181	21.471	43.214	-17.106	0.00	0.00	7
ATOM	1414	CA	SER	181	22.058	42.756	-18.365	0.00	0.00	6
ATOM	1415	CB	SER	181	23.453	42.206	-18.127	0.00	0.00	6
ATOM	1416	OG	SER	181	24.275	43.134	-17.462	0.00	0.00	8
ATOM	1417	C	SER	181	21.271	41.650	-19.020	0.00	0.00	6
ATOM	1418	O	SER	181	21.415	41.422	-20.215	0.00	0.00	8
ATOM	1419	N	SER	182	20.469	40.934	-18.242	0.00	0.00	7
ATOM	1420	CA	SER	182	19.716	39.839	-18.799	0.00	0.00	6
ATOM	1421	CB	SER	182	20.641	38.637	-18.997	0.00	0.00	6
ATOM	1422	OG	SER	182	19.892	37.518	-19.423	0.00	0.00	8
ATOM	1423	C	SER	182	18.557	39.448	-17.921	0.00	0.00	6

Figure 23.6

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ATOM	1424	O	SER	182	18.745	38.985	-16.806	0.00	0.00	8
ATOM	1425	N	TYR	183	17.354	39.590	-18.450	0.00	0.00	7
ATOM	1426	CA	TYR	183	16.165	39.240	-17.702	0.00	0.00	6
ATOM	1427	CB	TYR	183	14.922	39.574	-18.504	0.00	0.00	6
ATOM	1428	CG	TYR	183	14.706	41.046	-18.733	0.00	0.00	6
ATOM	1429	CD1	TYR	183	15.358	41.720	-19.769	0.00	0.00	6
ATOM	1430	CE1	TYR	183	15.136	43.095	-19.998	0.00	0.00	6
ATOM	1431	CD2	TYR	183	13.827	41.776	-17.930	0.00	0.00	6
ATOM	1432	CE2	TYR	183	13.594	43.152	-18.162	0.00	0.00	6
ATOM	1433	CZ	TYR	183	14.248	43.800	-19.195	0.00	0.00	6
ATOM	1434	OH	TYR	183	13.965	45.123	-19.446	0.00	0.00	8
ATOM	1435	C	TYR	183	16.152	37.765	-17.303	0.00	0.00	6
ATOM	1436	O	TYR	183	15.857	37.435	-16.157	0.00	0.00	8
ATOM	1437	N	GLU	184	16.503	36.888	-18.235	0.00	0.00	7
ATOM	1438	CA	GLU	184	16.518	35.453	-17.969	0.00	0.00	6
ATOM	1439	CB	GLU	184	16.814	34.658	-19.241	0.00	0.00	6
ATOM	1440	CG	GLU	184	16.886	33.140	-18.995	0.00	0.00	6
ATOM	1441	CD	GLU	184	16.499	32.303	-20.211	0.00	0.00	6
ATOM	1442	OE1	GLU	184	16.775	32.730	-21.350	0.00	0.00	8
ATOM	1443	OE2	GLU	184	15.923	31.207	-20.012	0.00	0.00	8
ATOM	1444	C	GLU	184	17.527	35.079	-16.909	0.00	0.00	6
ATOM	1445	O	GLU	184	17.227	34.308	-15.992	0.00	0.00	8
ATOM	1446	N	GLN	185	18.745	35.575	-17.061	0.00	0.00	7
ATOM	1447	CA	GLN	185	19.772	35.280	-16.089	0.00	0.00	6
ATOM	1448	CB	GLN	185	21.141	35.599	-16.634	0.00	0.00	6
ATOM	1449	CG	GLN	185	21.648	34.401	-17.374	0.00	0.00	6
ATOM	1450	CD	GLN	185	22.880	34.683	-18.133	0.00	0.00	6
ATOM	1451	OE1	GLN	185	23.157	35.818	-18.479	0.00	0.00	8
ATOM	1452	NE2	GLN	185	23.650	33.649	-18.401	0.00	0.00	7
ATOM	1453	C	GLN	185	19.534	35.908	-14.740	0.00	0.00	6
ATOM	1454	O	GLN	185	19.933	35.364	-13.723	0.00	0.00	8
ATOM	1455	N	ASN	186	18.803	37.006	-14.723	0.00	0.00	7
ATOM	1456	CA	ASN	186	18.492	37.660	-13.474	0.00	0.00	6
ATOM	1457	CB	ASN	186	17.961	39.071	-13.717	0.00	0.00	6
ATOM	1458	CG	ASN	186	17.954	39.896	-12.461	0.00	0.00	6
ATOM	1459	OD1	ASN	186	18.911	39.849	-11.687	0.00	0.00	8
ATOM	1460	ND2	ASN	186	16.904	40.668	-12.258	0.00	0.00	7
ATOM	1461	C	ASN	186	17.448	36.848	-12.721	0.00	0.00	6
ATOM	1462	O	ASN	186	17.591	36.612	-11.537	0.00	0.00	8
ATOM	1463	N	ASP	187	16.385	36.449	-13.413	0.00	0.00	7
ATOM	1464	CA	ASP	187	15.306	35.669	-12.829	0.00	0.00	6
ATOM	1465	CB	ASP	187	14.163	35.536	-13.837	0.00	0.00	6
ATOM	1466	CG	ASP	187	13.300	36.786	-13.931	0.00	0.00	6
ATOM	1467	OD1	ASP	187	13.622	37.809	-13.275	0.00	0.00	8
ATOM	1468	OD2	ASP	187	12.277	36.740	-14.656	0.00	0.00	8
ATOM	1469	C	ASP	187	15.697	34.272	-12.321	0.00	0.00	6
ATOM	1470	O	ASP	187	15.216	33.837	-11.275	0.00	0.00	8
ATOM	1471	N	ASN	188	16.506	33.546	-13.089	0.00	0.00	7
ATOM	1472	CA	ASN	188	16.924	32.187	-12.713	0.00	0.00	6
ATOM	1473	CB	ASN	188	17.620	31.448	-13.881	0.00	0.00	6
ATOM	1474	CG	ASN	188	16.659	31.067	-15.021	0.00	0.00	6
ATOM	1475	OD1	ASN	188	15.504	30.705	-14.798	0.00	0.00	8
ATOM	1476	ND2	ASN	188	17.147	31.172	-16.260	0.00	0.00	7
ATOM	1477	C	ASN	188	17.874	32.200	-11.521	0.00	0.00	6
ATOM	1478	O	ASN	188	17.812	31.330	-10.660	0.00	0.00	8
ATOM	1479	N	SER	189	18.813	33.133	-11.513	0.00	0.00	7
ATOM	1480	CA	SER	189	19.763	33.204	-10.418	0.00	0.00	6
ATOM	1481	CB	SER	189	20.983	34.036	-10.823	0.00	0.00	6
ATOM	1482	OG	SER	189	20.613	35.349	-11.194	0.00	0.00	8
ATOM	1483	C	SER	189	19.109	33.752	-9.136	0.00	0.00	6

Figure 23.7

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ATOM	1484	O	SER	189	19.513	33.410	-8.029	0.00	0.00	8
ATOM	1485	N	LEU	190	18.059	34.539	-9.287	0.00	0.00	7
ATOM	1486	CA	LEU	190	17.359	35.123	-8.145	0.00	0.00	6
ATOM	1487	CB	LEU	190	16.368	36.189	-8.628	0.00	0.00	6
ATOM	1488	CG	LEU	190	15.576	36.873	-7.522	0.00	0.00	6
ATOM	1489	CD1	LEU	190	16.557	37.491	-6.538	0.00	0.00	6
ATOM	1490	CD2	LEU	190	14.621	37.921	-8.103	0.00	0.00	6
ATOM	1491	C	LEU	190	16.622	34.060	-7.305	0.00	0.00	6
ATOM	1492	O	LEU	190	16.500	34.187	-6.089	0.00	0.00	8
ATOM	1493	N	VAL	191	16.099	33.029	-7.960	0.00	0.00	7
ATOM	1494	CA	VAL	191	15.397	31.964	-7.264	0.00	0.00	6
ATOM	1495	CB	VAL	191	14.585	31.109	-8.260	0.00	0.00	6
ATOM	1496	CG1	VAL	191	13.787	30.007	-7.541	0.00	0.00	6
ATOM	1497	CG2	VAL	191	13.586	32.016	-8.970	0.00	0.00	6
ATOM	1498	C	VAL	191	16.426	31.177	-6.465	0.00	0.00	6
ATOM	1499	O	VAL	191	16.215	30.897	-5.305	0.00	0.00	8
ATOM	1500	N	TYR	192	17.568	30.883	-7.061	0.00	0.00	7
ATOM	1501	CA	TYR	192	18.619	30.192	-6.341	0.00	0.00	6
ATOM	1502	CB	TYR	192	19.861	30.017	-7.232	0.00	0.00	6
ATOM	1503	CG	TYR	192	19.740	28.862	-8.188	0.00	0.00	6
ATOM	1504	CD1	TYR	192	19.292	29.057	-9.486	0.00	0.00	6
ATOM	1505	CE1	TYR	192	19.083	27.987	-10.339	0.00	0.00	6
ATOM	1506	CD2	TYR	192	19.988	27.555	-7.766	0.00	0.00	6
ATOM	1507	CE2	TYR	192	19.780	26.479	-8.608	0.00	0.00	6
ATOM	1508	CZ	TYR	192	19.324	26.703	-9.897	0.00	0.00	6
ATOM	1509	OH	TYR	192	19.110	25.652	-10.741	0.00	0.00	8
ATOM	1510	C	TYR	192	18.996	31.068	-5.159	0.00	0.00	6
ATOM	1511	O	TYR	192	19.161	30.577	-4.040	0.00	0.00	8
ATOM	1512	N	PHE	193	19.178	32.359	-5.445	0.00	0.00	7
ATOM	1513	CA	PHE	193	19.562	33.354	-4.461	0.00	0.00	6
ATOM	1514	CB	PHE	193	19.555	34.762	-5.087	0.00	0.00	6
ATOM	1515	CG	PHE	193	20.179	35.836	-4.213	0.00	0.00	6
ATOM	1516	CD1	PHE	193	21.454	36.306	-4.480	0.00	0.00	6
ATOM	1517	CD2	PHE	193	19.473	36.385	-3.130	0.00	0.00	6
ATOM	1518	CE1	PHE	193	22.035	37.308	-3.696	0.00	0.00	6
ATOM	1519	CE2	PHE	193	20.043	37.395	-2.331	0.00	0.00	6
ATOM	1520	CZ	PHE	193	21.325	37.854	-2.618	0.00	0.00	6
ATOM	1521	C	PHE	193	18.589	33.280	-3.315	0.00	0.00	6
ATOM	1522	O	PHE	193	18.991	33.125	-2.175	0.00	0.00	8
ATOM	1523	N	ALA	194	17.309	33.328	-3.631	0.00	0.00	7
ATOM	1524	CA	ALA	194	16.274	33.290	-2.619	0.00	0.00	6
ATOM	1525	CB	ALA	194	14.902	33.295	-3.278	0.00	0.00	6
ATOM	1526	C	ALA	194	16.430	32.089	-1.677	0.00	0.00	6
ATOM	1527	O	ALA	194	16.449	32.244	-0.451	0.00	0.00	8
ATOM	1528	N	TYR	195	16.633	30.906	-2.237	0.00	0.00	7
ATOM	1529	CA	TYR	195	16.770	29.709	-1.416	0.00	0.00	6
ATOM	1530	CB	TYR	195	16.754	28.455	-2.297	0.00	0.00	6
ATOM	1531	CG	TYR	195	16.807	27.147	-1.518	0.00	0.00	6
ATOM	1532	CD1	TYR	195	15.793	26.795	-0.622	0.00	0.00	6
ATOM	1533	CE1	TYR	195	15.881	25.625	0.136	0.00	0.00	6
ATOM	1534	CD2	TYR	195	17.899	26.283	-1.645	0.00	0.00	6
ATOM	1535	CE2	TYR	195	17.986	25.099	-0.895	0.00	0.00	6
ATOM	1536	CZ	TYR	195	16.983	24.787	-0.006	0.00	0.00	6
ATOM	1537	OH	TYR	195	17.120	23.664	0.771	0.00	0.00	8
ATOM	1538	C	TYR	195	18.019	29.712	-0.541	0.00	0.00	6
ATOM	1539	O	TYR	195	17.948	29.581	0.685	0.00	0.00	8
ATOM	1540	N	TYR	196	19.165	29.887	-1.178	0.00	0.00	7
ATOM	1541	CA	TYR	196	20.421	29.865	-0.475	0.00	0.00	6
ATOM	1542	CB	TYR	196	21.585	29.653	-1.453	0.00	0.00	6
ATOM	1543	CG	TYR	196	21.526	28.262	-2.071	0.00	0.00	6

Figure 23.8

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ATOM	1544	CD1	TYR	196	20.932	28.057	-3.327	0.00	0.00	6
ATOM	1545	CE1	TYR	196	20.744	26.773	-3.846	0.00	0.00	6
ATOM	1546	CD2	TYR	196	21.951	27.121	-1.355	0.00	0.00	6
ATOM	1547	CE2	TYR	196	21.769	25.826	-1.878	0.00	0.00	6
ATOM	1548	CZ	TYR	196	21.155	25.674	-3.117	0.00	0.00	6
ATOM	1549	OH	TYR	196	20.864	24.438	-3.599	0.00	0.00	8
ATOM	1550	C	TYR	196	20.640	31.013	0.479	0.00	0.00	6
ATOM	1551	O	TYR	196	21.617	31.000	1.222	0.00	0.00	8
ATOM	1552	N	HIS	197	19.760	32.020	0.434	0.00	0.00	7
ATOM	1553	CA	HIS	197	19.845	33.145	1.366	0.00	0.00	6
ATOM	1554	CB	HIS	197	19.837	34.508	0.655	0.00	0.00	6
ATOM	1555	CG	HIS	197	21.117	34.805	-0.067	0.00	0.00	6
ATOM	1556	CD2	HIS	197	21.637	34.292	-1.208	0.00	0.00	6
ATOM	1557	ND1	HIS	197	22.062	35.673	0.425	0.00	0.00	7
ATOM	1558	CE1	HIS	197	23.116	35.679	-0.375	0.00	0.00	6
ATOM	1559	NE2	HIS	197	22.884	34.848	-1.373	0.00	0.00	7
ATOM	1560	C	HIS	197	18.781	33.008	2.455	0.00	0.00	6
ATOM	1561	O	HIS	197	18.656	33.855	3.338	0.00	0.00	8
=====	=====	=====	=====	=====	=====	=====	=====	=====	=====	=
ATOM	1779	N	LEU	226	2.352	24.910	-15.190	0.00	0.00	7
ATOM	1780	CA	LEU	226	1.463	25.680	-14.329	0.00	0.00	6
ATOM	1781	CB	LEU	226	0.022	25.288	-14.600	0.00	0.00	6
ATOM	1782	CG	LEU	226	-0.385	25.876	-15.950	0.00	0.00	6
ATOM	1783	CD1	LEU	226	-1.496	25.041	-16.590	0.00	0.00	6
ATOM	1784	CD2	LEU	226	-0.802	27.332	-15.735	0.00	0.00	6
ATOM	1785	C	LEU	226	1.743	25.695	-12.833	0.00	0.00	6
ATOM	1786	O	LEU	226	1.491	26.698	-12.166	0.00	0.00	8
ATOM	1787	N	GLU	227	2.227	24.583	-12.296	0.00	0.00	7
ATOM	1788	CA	GLU	227	2.548	24.524	-10.874	0.00	0.00	6
ATOM	1789	CB	GLU	227	2.532	23.086	-10.383	0.00	0.00	6
ATOM	1790	CG	GLU	227	1.139	22.494	-10.521	0.00	0.00	6
ATOM	1791	CD	GLU	227	1.019	21.103	-9.943	0.00	0.00	6
ATOM	1792	OE1	GLU	227	0.888	20.998	-8.699	0.00	0.00	8
ATOM	1793	OE2	GLU	227	1.048	20.124	-10.734	0.00	0.00	8
ATOM	1794	C	GLU	227	3.889	25.207	-10.631	0.00	0.00	6
ATOM	1795	O	GLU	227	4.097	25.850	-9.602	0.00	0.00	8
ATOM	1796	N	CYS	228	4.775	25.097	-11.611	0.00	0.00	7
ATOM	1797	CA	CYS	228	6.062	25.758	-11.560	0.00	0.00	6
ATOM	1798	C	CYS	228	5.799	27.269	-11.508	0.00	0.00	6
ATOM	1799	O	CYS	228	6.400	27.994	-10.734	0.00	0.00	8
ATOM	1800	CB	CYS	228	6.840	25.463	-12.812	0.00	0.00	6
ATOM	1801	SG	CYS	228	8.238	26.583	-12.943	0.00	0.00	16
ATOM	1802	N	VAL	229	4.870	27.729	-12.331	0.00	0.00	7
ATOM	1803	CA	VAL	229	4.492	29.131	-12.370	0.00	0.00	6
ATOM	1804	CB	VAL	229	3.510	29.402	-13.531	0.00	0.00	6
ATOM	1805	CG1	VAL	229	2.830	30.758	-13.367	0.00	0.00	6
ATOM	1806	CG2	VAL	229	4.248	29.311	-14.858	0.00	0.00	6
ATOM	1807	C	VAL	229	3.869	29.539	-11.039	0.00	0.00	6
ATOM	1808	O	VAL	229	4.072	30.652	-10.577	0.00	0.00	8
ATOM	1809	N	THR	230	3.085	28.656	-10.436	0.00	0.00	7
ATOM	1810	CA	THR	230	2.461	28.950	-9.142	0.00	0.00	6
ATOM	1811	CB	THR	230	1.448	27.841	-8.748	0.00	0.00	6
ATOM	1812	OG1	THR	230	0.497	27.680	-9.808	0.00	0.00	8
ATOM	1813	CG2	THR	230	0.688	28.211	-7.486	0.00	0.00	6
ATOM	1814	C	THR	230	3.555	29.111	-8.069	0.00	0.00	6
ATOM	1815	O	THR	230	3.474	29.988	-7.197	0.00	0.00	8
ATOM	1816	N	ASN	231	4.600	28.295	-8.172	0.00	0.00	7
ATOM	1817	CA	ASN	231	5.719	28.372	-7.253	0.00	0.00	6
ATOM	1818	CB	ASN	231	6.628	27.166	-7.428	0.00	0.00	6
ATOM	1819	CG	ASN	231	5.975	25.877	-6.984	0.00	0.00	6

Figure 23.9

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ATOM	1820	OD1	ASN	231	6.433	24.799	-7.349	0.00	0.00	8
ATOM	1821	ND2	ASN	231	4.912	25.972	-6.187	0.00	0.00	7
ATOM	1822	C	ASN	231	6.511	29.661	-7.493	0.00	0.00	6
ATOM	1823	O	ASN	231	6.833	30.370	-6.543	0.00	0.00	8
ATOM	1824	N	LEU	232	6.838	29.946	-8.757	0.00	0.00	7
ATOM	1825	CA	LEU	232	7.572	31.165	-9.123	0.00	0.00	6
ATOM	1826	CB	LEU	232	7.903	31.194	-10.608	0.00	0.00	6
ATOM	1827	CG	LEU	232	8.945	30.168	-11.006	0.00	0.00	6
ATOM	1828	CD1	LEU	232	9.161	30.243	-12.517	0.00	.0.00	6
ATOM	1829	CD2	LEU	232	10.235	30.440	-10.257	0.00	0.00	6
ATOM	1830	C	LEU	232	6.821	32.435	-8.719	0.00	0.00	6
ATOM	1831	O	LEU	232	7.439	33.410	-8.328	0.00	0.00	8
ATOM	1832	N	GLN	233	5.502	32.429	-8.785	0.00	0.00	7
ATOM	1833	CA	GLN	233	4.748	33.601	-8.364	0.00	0.00	6
ATOM	1834	CB	GLN	233	3.275	33.477	-8.749	0.00	0.00	6
ATOM	1835	CG	GLN	233	2.983	33.724	-10.239	0.00	0.00	6
ATOM	1836	CD	GLN	233	1.541	33.424	-10.596	0.00	0.00	6
ATOM	1837	OE1	GLN	233	0.909	34.149	-11.371	0.00	0.00 ·	8
ATOM	1838	NE2	GLN	233	1.008	32.348	-10.028	0.00	0.00	7
ATOM	1839	C	GLN	233	4.901	33.816	-6.850	0.00	0.00	6
ATOM	1840	O	GLN	233	4.820	34.961	-6.365	0.00	0.00	8
ATOM	1841	N	GLU	234	5.120	32.722	-6.113	0.00	0.00	7
ATOM	1842	CA	GLU	234	5.311	32.767	-4.660	0.00	0.00	6
ATOM	1843	CB	GLU	234	5.132	31.382	-4.040	0.00	0.00	6
ATOM	1844	CG	GLU	234	5.527	31.310	-2.556	0.00	0.00	6
ATOM	1845	CD	GLU	234	4.629	32.135	-1.615	0.00	0.00	6
ATOM	1846	OE1	GLU	234	3.659	32.805	-2.049	0.00	0.00	8
ATOM	1847	OE2	GLU	234	4.896	32.100	-0.396	0.00	0.00	8
ATOM	1848	C	GLU	234	6.704	33.267	-4.335	0.00	0.00	6
ATOM	1849	O	GLU	234	6.923	33.956	-3.342	0.00	0.00	8
ATOM	1850	N	VAL	235	7.665	32.832	-5.126	0.00	0.00	7
ATOM	1851	CA	VAL	235	9.018	33.293	-4.952	0.00	0.00	6
ATOM	1852	CB	VAL	235	9.927	32.575	-5.925	0.00	0.00	6
ATOM	1853	CG1	VAL	235	11.347	33.107	-5.808	0.00	0.00	6
ATOM	1854	CG2	VAL	235	9.862	31.077	-5.668	0.00	0.00	6
ATOM	1855	C	VAL	235	9.076	34.827	-5.208	0.00	0.00	6
ATOM	1856	O	VAL	235	9.716	35.580	-4.464	0.00	0.00	8
ATOM	1857	N	ALA	236	8.372	35.286	-6.241	0.00	0.00	7
ATOM	1858	CA	ALA	236	8.332	36.712	-6.600	0.00	0.00	6
ATOM	1859	CB	ALA	236	7.527	36.908	-7.877	0.00	0.00	6
ATOM	1860	C	ALA	236	7.718	37.538	-5.472	0.00	0.00	6
ATOM	1861	O	ALA	236	8.168	38.650	-5.202	0.00	0.00 ·	8
ATOM	1862	N	ARG	237	6.680	36.997	-4.830	0.00	0.00	7
ATOM	1863	CA	ARG	237	5.996	37.660	-3.714	0.00	0.00	6
ATOM	1864	CB	ARG	237	4.754	36.878	-3.301	0.00	0.00	6
ATOM	1865	CG	ARG	237	4.043	37.521	-2.130	0.00	0.00	6
ATOM	1866	CD	ARG	237	3.006	36.601	-1.550	0.00	0.00	6
ATOM	1867	NE	ARG	237	3.614	35.536	-0.759	0.00	0.00	7
ATOM	1868	CZ	ARG	237	4.155	35.721	0.437	0.00	0.00	6
ATOM	1869	NH1	ARG	237	4.164	36.928	0.977	0.00	0.00	7 ·
ATOM	1870	NH2	ARG	237	4.692	34.700	1.083	0.00	0.00	7
ATOM	1871	C	ARG	237	6.890	37.801	-2.488	0.00	0.00	6
ATOM	1872	O	ARG	237	6.926	38.845	-1.841	0.00	0.00	8
ATOM	1873	N	ILE	238	7.593	36.733	-2.147	0.00	0.00	7
ATOM	1874	CA	ILE	238	8.464	36.760	-0.985	0.00	0.00	6
ATOM	1875	CB	ILE	238	9.048	35.358	-0.686	0.00	0.00	6
ATOM	1876	CG2	ILE	238	10.144	35.452	0.384	0.00	0.00	6
ATOM	1877	CG1	ILE	238	7.920	34.377	-0.346	0.00	0.00	6
ATOM	1878	CD1	ILE	238	8.357	32.935	-0.401	0.00	0.00	6
ATOM	1879	C	ILE	238	9.594	37.751	-1.219	0.00	0.00	6

Figure 23.10

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ATOM	1880	O	ILE	238	9.876	38.585	-0.360	0.00	0.00	8
ATOM	1881	N	VAL	239	10.216	37.685	-2.394	0.00	0.00	7
ATOM	1882	CA	VAL	239	11.327	38.583	-2.715	0.00	0.00	6
ATOM	1883	CB	VAL	239	12.052	38.202	-4.052	0.00	0.00	6
ATOM	1884	CG1	VAL	239	13.025	39.311	-4.462	0.00	0.00	6
ATOM	1885	CG2	VAL	239	12.810	36.889	-3.909	0.00	0.00	6
ATOM	1886	C	VAL	239	10.950	40.051	-2.805	0.00	0.00	6
ATOM	1887	O	VAL	239	11.623	40.886	-2.216	0.00	0.00	8
ATOM	1888	N	GLY	240	9.878	40.372	-3.527	0.00	0.00	7
ATOM	1889	CA	GLY	240	9.523	41.768	-3.704	0.00	0.00	6
ATOM	1890	C	GLY	240	8.227	42.287	-3.154	0.00	0.00	6
ATOM	1891	O	GLY	240	7.888	43.441	-3.396	0.00	0.00	8
ATOM	1892	N	ASN	241	7.503	41.475	-2.399	0.00	0.00	7
ATOM	1893	CA	ASN	241	6.243	41.945	-1.854	0.00	0.00	6
ATOM	1894	CB	ASN	241	5.117	41.666	-2.853	0.00	0.00	6
ATOM	1895	CG	ASN	241	3.879	42.498	-2.594	0.00	0.00	6
ATOM	1896	OD1	ASN	241	2.762	42.047	-2.865	0.00	0.00	8
ATOM	1897	ND2	ASN	241	4.063	43.735	-2.102	0.00	0.00	7
ATOM	1898	C	ASN	241	5.914	41.355	-0.488	0.00	0.00	6
ATOM	1899	O	ASN	241	4.754	41.107	-0.183	0.00	0.00	8
ATOM	1900	N	SER	242	6.931	41.168	0.348	0.00	0.00	7
ATOM	1901	CA	SER	242	6.706	40.614	1.686	0.00	0.00	6
ATOM	1902	CB	SER	242	7.240	39.176	1.763	0.00	0.00	5
ATOM	1903	OG	SER	242	8.648	39.160	1.867	0.00	0.00	8
ATOM	1904	C	SER	242	7.258	41.448	2.864	0.00	0.00	6
ATOM	1905	O	SER	242	7.038	41.096	4.023	0.00	0.00	8
ATOM	1906	N	GLY	243	7.943	42.552	2.568	0.00	0.00	7
ATOM	1907	CA	GLY	243	8.512	43.380	3.610	0.00	0.00	6
ATOM	1908	C	GLY	243	10.021	43.394	3.574	0.00	0.00	6
ATOM	1909	O	GLY	243	10.667	44.122	4.307	0.00	0.00	8
ATOM	1910	N	LEU	244	10.604	42.545	2.749	0.00	0.00	7
ATOM	1911	CA	LEU	244	12.050	42.502	2.620	0.00	0.00	6
ATOM	1912	CB	LEU	244	12.537	41.145	2.067	0.00	0.00	6
ATOM	1913	CG	LEU	244	12.208	39.814	2.778	0.00	0.00	6
ATOM	1914	CD1	LEU	244	12.508	38.640	1.852	0.00	0.00	6
ATOM	1915	CD2	LEU	244	13.009	39.696	4.071	0.00	0.00	6
ATOM	1916	C	LEU	244	12.399	43.598	1.617	0.00	0.00	6
ATOM	1917	O	LEU	244	11.609	43.936	0.713	0.00	0.00	8
ATOM	1918	N	ASN	245	13.579	44.162	1.816	0.00	0.00	7
ATOM	1919	CA	ASN	245	14.114	45.189	0.959	0.00	0.00	6
ATOM	1920	CB	ASN	245	15.053	46.064	1.789	0.00	0.00	6
ATOM	1921	CG	ASN	245	15.593	47.246	1.019	0.00	0.00	6
ATOM	1922	OD1	ASN	245	15.664	47.219	-0.210	0.00	0.00	8
ATOM	1923	ND2	ASN	245	16.028	48.275	1.743	0.00	0.00	7
ATOM	1924	C	ASN	245	14.871	44.471	-0.180	0.00	0.00	6
ATOM	1925	O	ASN	245	15.938	43.878	0.019	0.00	0.00	8
ATOM	1926	N	ILE	246	14.309	44.560	-1.383	0.00	0.00	7
ATOM	1927	CA	ILE	246	14.888	43.913	-2.562	0.00	0.00	6
ATOM	1928	CB	ILE	246	13.872	43.930	-3.740	0.00	0.00	6
ATOM	1929	CG2	ILE	246	13.701	45.363	-4.312	0.00	0.00	6
ATOM	1930	CG1	ILE	246	14.306	42.918	-4.792	0.00	0.00	6
ATOM	1931	CD1	ILE	246	13.305	42.730	-5.875	0.00	0.00	6
ATOM	1932	C	ILE	246	16.261	44.428	-2.959	0.00	0.00	6
ATOM	1933	O	ILE	246	17.053	43.722	-3.580	0.00	0.00	8
ATOM	1934	N	TYR	247	16.575	45.652	-2.551	0.00	0.00	7
ATOM	1935	CA	TYR	247	17.875	46.252	-2.836	0.00	0.00	6
ATOM	1936	CB	TYR	247	17.789	47.780	-2.804	0.00	0.00	6
ATOM	1937	CG	TYR	247	17.100	48.426	-3.981	0.00	0.00	6
ATOM	1938	CD1	TYR	247	16.687	47.679	-5.079	0.00	0.00	6
ATOM	1939	CE1	TYR	247	16.107	48.291	-6.179	0.00	0.00	6

Figure 23.11

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ATOM	1940	CD2	TYR	247	16.904	49.811	-4.023	0.00	0.00	6
ATOM	1941	CE2	TYR	247	16.335	50.421	-5.111	0.00	0.00	6
ATOM	1942	CZ	TYR	247	15.941	49.659	-6.189	0.00	0.00	6
ATOM	1943	OH	TYR	247	15.411	50.250	-7.306	0.00	0.00	8
ATOM	1944	C	TYR	247	18.969	45.831	-1.847	0.00	0.00	6
ATOM	1945	O	TYR	247	20.153	46.087	-2.056	0.00	0.00	8
ATOM	1946	N	ASN	248	18.584	45.227	-0.741	0.00	0.00	7
ATOM	1947	CA	ASN	248	19.579	44.834	0.241	0.00	0.00	6
ATOM	1948	CB	ASN	248	20.107	46.057	0.971	0.00	0.00	6
ATOM	1949	CG	ASN	248	21.294	45.739	1.824	0.00	0.00	6
ATOM	1950	OD1	ASN	248	21.349	44.701	2.461	0.00	0.00	8
ATOM	1951	ND2	ASN	248	22.273	46.610	1.812	0.00	0.00	7
ATOM	1952	C	ASN	248	18.827	43.940	1.178	0.00	0.00	6
ATOM	1953	O	ASN	248	17.964	44.401	1.916	0.00	0.00	8
ATOM	1954	N	LEU	249	19.094	42.645	1.091	0.00	0.00	7
ATOM	1955	CA	LEU	249	18.384	41.674	1.911	0.00	0.00	6
ATOM	1956	CB	LEU	249	18.824	40.251	1.503	0.00	0.00	6
ATOM	1957	CG	LEU	249	18.163	39.074	2.235	0.00	0.00	6
ATOM	1958	CD1	LEU	249	16.675	39.049	1.987	0.00	0.00	6
ATOM	1959	CD2	LEU	249	18.809	37.771	1.812	0.00	0.00	6
ATOM	1960	C	LEU	249	18.548	41.899	3.431	0.00	0.00	6
ATOM	1961	O	LEU	249	17.593	41.769	4.199	0.00	0.00	8
ATOM	1962	N	TYR	250	19.744	42.319	3.840	0.00	0.00	7
ATOM	1963	CA	TYR	250	20.070	42.499	5.249	0.00	0.00	6
ATOM	1964	CB	TYR	250	21.507	42.075	5.456	0.00	0.00	6
ATOM	1965	CG	TYR	250	21.696	40.673	4.951	0.00	0.00	6
ATOM	1966	CD1	TYR	250	22.611	40.392	3.942	0.00	0.00	6
ATOM	1967	CE1	TYR	250	22.736	39.107	3.417	0.00	0.00	6
ATOM	1968	CD2	TYR	250	20.906	39.636	5.435	0.00	0.00	6
ATOM	1969	CE2	TYR	250	21.026	38.333	4.915	0.00	0.00	6
ATOM	1970	CZ	TYR	250	21.950	38.070	3.901	0.00	0.00	6
ATOM	1971	OH	TYR	250	22.115	36.782	3.399	0.00	0.00	8
ATOM	1972	C	TYR	250	19.829	43.878	5.820	0.00	0.00	6
ATOM	1973	O	TYR	250	20.307	44.211	6.899	0.00	0.00	8
ATOM	1974	N	ALA	251	19.013	44.638	5.110	0.00	0.00	7
ATOM	1975	CA	ALA	251	18.682	45.978	5.504	0.00	0.00	6
ATOM	1976	CB	ALA	251	19.211	46.984	4.478	0.00	0.00	6
ATOM	1977	C	ALA	251	17.184	46.107	5.662	0.00	0.00	6
ATOM	1978	O	ALA	251	16.402	45.368	5.046	0.00	0.00	8
ATOM	1979	N	PRO	252	16.761	47.014	6.558	0.00	0.00	7
ATOM	1980	CD	PRO	252	17.590	47.925	7.376	0.00	0.00	6
ATOM	1981	CA	PRO	252	15.343	47.259	6.815	0.00	0.00	6
ATOM	1982	CB	PRO	252	15.382	48.209	8.018	0.00	0.00	6
ATOM	1983	CG	PRO	252	16.596	49.021	7.741	0.00	0.00	6
ATOM	1984	C	PRO	252	14.705	47.930	5.594	0.00	0.00	6
ATOM	1985	O	PRO	252	15.398	48.442	4.703	0.00	0.00	8
ATOM	1986	N	CYS	253	13.383	47.905	5.573	0.00	0.00	7
ATOM	1987	CA	CYS	253	12.599	48.492	4.523	0.00	0.00	6
ATOM	1988	C	CYS	253	12.128	49.812	5.106	0.00	0.00	6
ATOM	1989	O	CYS	253	11.530	49.824	6.180	0.00	0.00	8
ATOM	1990	CB	CYS	253	11.421	47.563	4.204	0.00	0.00	6
ATOM	1991	SG	CYS	253	10.314	48.110	2.865	0.00	0.00	16
ATOM	1992	N	ALA	254	12.481	50.919	4.451	0.00	0.00	7
ATOM	1993	CA	ALA	254	12.072	52.252	4.903	0.00	0.00	6
ATOM	1994	CB	ALA	254	12.501	53.319	3.913	0.00	0.00	6
ATOM	1995	C	ALA	254	10.561	52.278	5.090	0.00	0.00	6
ATOM	1996	O	ALA	254	9.808	52.014	4.148	0.00	0.00	8
ATOM	1997	N	GLY	255	10.122	52.568	6.312	0.00	0.00	7
ATOM	1998	CA	GLY	255	8.697	52.590	6.579	0.00	0.00	6
ATOM	1999	C	GLY	255	8.186	51.275	7.148	0.00	0.00	6

Figure 23.12

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ATOM	2000	O	GLY	255	6.991	51.117	7.409	0.00	0.00	8
ATOM	2001	N	GLY	256	9.080	50.316	7.322	0.00	0.00	7
ATOM	2002	CA	GLY	256	8.672	49.051	7.887	0.00	0.00	6
ATOM	2003	C	GLY	256	7.810	48.165	7.016	0.00	0.00	6
ATOM	2004	O	GLY	256	7.610	48.417	5.825	0.00	0.00	8
ATOM	2005	N	VAL	257	7.334	47.088	7.632	0.00	0.00	7
ATOM	2006	CA	VAL	257	6.489	46.094	6.977	0.00	0.00	6
ATOM	2007	CB	VAL	257	6.907	44.664	7.384	0.00	0.00	6
ATOM	2008	CG1	VAL	257	5.968	43.641	6.791	0.00	0.00	6
ATOM	2009	CG2	VAL	257	8.318	44.394	6.934	0.00	0.00	6
ATOM	2010	C	VAL	257	5.026	46.323	7.346	0.00	0.00	6
ATOM	2011	O	VAL	257	4.678	46.411	8.535	0.00	0.00	8
ATOM	2012	N	PRO	258	4.165	46.487	6.325	0.00	0.00	7
ATOM	2013	CD	PRO	258	4.580	46.636	4.916	0.00	0.00	6
ATOM	2014	CA	PRO	258	2.721	46.716	6.470	0.00	0.00	6
ATOM	2015	CB	PRO	258	2.297	47.095	5.048	0.00	0.00	6
ATOM	2016	CG	PRO	258	3.304	46.399	4.186	0.00	0.00	6
ATOM	2017	C	PRO	258	1.922	45.507	7.000	0.00	0.00	6
ATOM	2018	OT1	PRO	258	2.338	44.354	6.738	0.00	0.00	8
ATOM	2019	OT2	PRO	258	0.882	45.733	7.681	0.00	0.00	8
TER										
ATOM	2020	CB	ALA	261	-0.009	50.908	-0.677	0.00	0.00	6
ATOM	2021	C	ALA	261	1.573	52.567	0.349	0.00	0.00	6
ATOM	2022	O	ALA	261	0.678	52.779	1.163	0.00	0.00	8
ATOM	2023	N	ALA	261	2.399	50.298	-0.348	0.00	0.00	7
ATOM	2024	CA	ALA	261	1.453	51.418	-0.640	0.00	0.00	6
ATOM	2025	N	ARG	262	2.680	53.297	0.309	0.00	0.00	7
ATOM	2026	CA	ARG	262	2.834	54.443	1.209	0.00	0.00	6
ATOM	2027	CB	ARG	262	4.240	55.067	1.099	0.00	0.00	6
ATOM	2028	CG	ARG	262	5.417	54.108	1.424	0.00	0.00	6
ATOM	2029	CD	ARG	262	6.775	54.691	0.940	0.00	0.00	6
ATOM	2030	NE	ARG	262	7.188	55.907	1.671	0.00	0.00	7
ATOM	2031	CZ	ARG	262	8.165	56.741	1.285	0.00	0.00	6
ATOM	2032	NH1	ARG	262	8.847	56.506	0.155	0.00	0.00	7
ATOM	2033	NH2	ARG	262	8.482	57.794	2.055	0.00	0.00	7
ATOM	2034	C	ARG	262	1.813	55.440	0.695	0.00	0.00	6
ATOM	2035	O	ARG	262	1.630	55.597	-0.512	0.00	0.00	8
ATOM	2036	N	ALA	263	1.070	56.036	1.605	0.00	0.00	7
ATOM	2037	CA	ALA	263	0.080	57.022	1.205	0.00	0.00	6
ATOM	2038	CB	ALA	263	-1.296	56.693	1.798	0.00	0.00	6
ATOM	2039	C	ALA	263	0.630	58.295	1.802	0.00	0.00	6
ATOM	2040	O	ALA	263	1.264	58.265	2.881	0.00	0.00	8
ATOM	2041	N	GLU	264	0.472	59.398	1.081	0.00	0.00	7
ATOM	2042	CA	GLU	264	0.992	60.638	1.590	0.00	0.00	6
ATOM	2043	CB	GLU	264	2.256	61.005	0.831	0.00	0.00	6
ATOM	2044	CG	GLU	264	3.211	59.827	0.776	0.00	0.00	6
ATOM	2045	CD	GLU	264	4.656	60.243	0.654	0.00	0.00	6
ATOM	2046	OE1	GLU	264	4.923	61.325	0.053	0.00	0.00	8
ATOM	2047	OE2	GLU	264	5.528	59.485	1.175	0.00	0.00	8
ATOM	2048	C	GLU	264	-0.054	61.735	1.542	0.00	0.00	6
ATOM	2049	O	GLU	264	0.290	62.938	1.510	0.00	0.00	8
ATOM	2050	N	ALA	265	-1.319	61.309	1.657	0.00	0.00	7
ATOM	2051	CA	ALA	265	-2.479	62.210	1.643	0.00	0.00	6
ATOM	2052	CB	ALA	265	-2.304	63.354	2.656	0.00	0.00	6
ATOM	2053	C	ALA	265	-2.674	62.761	0.244	0.00	0.00	6
ATOM	2054	O	ALA	265	-2.042	63.746	-0.147	0.00	0.00	8
ATOM	2055	N	ASP	266	-3.558	62.096	-0.493	0.00	0.00	7
ATOM	2056	CA	ASP	266	-3.858	62.447	-1.875	0.00	0.00	6
ATOM	2057	CB	ASP	266	-4.058	63.957	-2.035	0.00	0.00	6
ATOM	2058	CG	ASP	266	-5.223	64.479	-1.208	0.00	0.00	6

Figure 23.13

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ATOM	2059	OD1	ASP	266	-5.856	63.689	-0.455	0.00	0.00	8
ATOM	2060	OD2	ASP	266	-5.510	65.689	-1.321	0.00	0.00	8
ATOM	2061	C	ASP	266	-2.747	61.960	-2.792	0.00	0.00	6
ATOM	2062	O	ASP	266	-2.685	62.352	-3.953	0.00	0.00	8
ATOM	2063	N	THR	267	-1.888	61.090	-2.263	0.00	0.00	7
ATOM	2064	CA	THR	267	-0.780	60.535	-3.026	0.00	0.00	6
ATOM	2065	CB	THR	267	0.565	61.234	-2.730	0.00	0.00	6
ATOM	2066	OG1	THR	267	0.547	62.571	-3.246	0.00	0.00	8
ATOM	2067	CG2	THR	267	1.714	60.471	-3.377	0.00	0.00	6
ATOM	2068	C	THR	267	-0.589	59.090	-2.657	0.00	0.00	6
ATOM	2069	O	THR	267	-0.277	58.775	-1.500	0.00	0.00	8
ATOM	2070	N	VAL	268	-0.807	58.218	-3.634	0.00	0.00	7
ATOM	2071	CA	VAL	268	-0.604	56.789	-3.451	0.00	0.00	6
ATOM	2072	CB	VAL	268	-1.566	55.980	-4.329	0.00	0.00	6
ATOM	2073	CG1	VAL	268	-1.153	54.535	-4.362	0.00	0.00	6
ATOM	2074	CG2	VAL	268	-2.961	56.107	-3.796	0.00	0.00	6
ATOM	2075	C	VAL	268	0.823	56.557	-3.919	0.00	0.00	6
ATOM	2076	O	VAL	268	1.207	57.046	-4.980	0.00	0.00	8
ATOM	2077	N	VAL	269	1.635	55.897	-3.110	0.00	0.00	7
ATOM	2078	CA	VAL	269	3.006	55.649	-3.512	0.00	0.00	6
ATOM	2079	CB	VAL	269	4.025	55.941	-2.375	0.00	0.00	6
ATOM	2080	CG1	VAL	269	5.437	55.724	-2.860	0.00	0.00	6
ATOM	2081	CG2	VAL	269	3.894	57.366	-1.913	0.00	0.00	6
ATOM	2082	C	VAL	269	3.088	54.196	-3.961	0.00	0.00	6
ATOM	2083	O	VAL	269	2.609	53.294	-3.279	0.00	0.00	8
ATOM	2084	N	VAL	270	3.634	53.987	-5.150	0.00	0.00	7
ATOM	2085	CA	VAL	270	3.784	52.660	-5.733	0.00	0.00	6
ATOM	2086	CB	VAL	270	3.143	52.594	-7.155	0.00	0.00	6
ATOM	2087	CG1	VAL	270	3.578	51.343	-7.884	0.00	0.00	6
ATOM	2088	CG2	VAL	270	1.634	52.596	-7.022	0.00	0.00	6
ATOM	2089	C	VAL	270	5.274	52.440	-5.804	0.00	0.00	6
ATOM	2090	O	VAL	270	6.017	53.391	-6.003	0.00	0.00	8
ATOM	2091	N	GLN	271	5.718	51.204	-5.597	0.00	0.00	7
ATOM	2092	CA	GLN	271	7.152	50.896	-5.613	0.00	0.00	6
ATOM	2093	CB	GLN	271	7.621	50.532	-4.204	0.00	0.00	6
ATOM	2094	CG	GLN	271	7.301	51.578	-3.157	0.00	0.00	6
ATOM	2095	CD	GLN	271	8.131	51.420	-1.877	0.00	0.00	6
ATOM	2096	OE1	GLN	271	8.438	50.290	-1.443	0.00	0.00	8
ATOM	2097	NE2	GLN	271	8.516	52.559	-1.273	0.00	0.00	7
ATOM	2098	C	GLN	271	7.534	49.769	-6.575	0.00	0.00	6
ATOM	2099	O	GLN	271	8.579	49.168	-6.416	0.00	0.00	8
ATOM	2100	N	ASP	272	6.741	49.553	-7.621	0.00	0.00	7
ATOM	2101	CA	ASP	272	6.991	48.479	-8.573	0.00	0.00	6
ATOM	2102	CB	ASP	272	5.663	47.737	-8.815	0.00	0.00	6
ATOM	2103	CG	ASP	272	5.785	46.584	-9.784	0.00	0.00	6
ATOM	2104	OD1	ASP	272	6.887	46.018	-9.923	0.00	0.00	8
ATOM	2105	OD2	ASP	272	4.765	46.252	-10.414	0.00	0.00	8
ATOM	2106	C	ASP	272	7.602	49.000	-9.875	0.00	0.00	6
ATOM	2107	O	ASP	272	6.895	49.474	-10.753	0.00	0.00	8
ATOM	2108	N	LEU	273	8.918	48.904	-9.999	0.00	0.00	7
ATOM	2109	CA	LEU	273	9.605	49.376	-11.188	0.00	0.00	6
ATOM	2110	CB	LEU	273	11.085	49.625	-10.894	0.00	0.00	6
ATOM	2111	CG	LEU	273	11.446	50.578	-9.748	0.00	0.00	6
ATOM	2112	CD1	LEU	273	12.895	50.870	-9.815	0.00	0.00	6
ATOM	2113	CD2	LEU	273	10.703	51.843	-9.826	0.00	0.00	6
ATOM	2114	C	LEU	273	9.426	48.467	-12.416	0.00	0.00	6
ATOM	2115	O	LEU	273	9.729	48.883	-13.533	0.00	0.00	8
ATOM	2116	N	GLY	274	8.984	47.224	-12.192	0.00	0.00	7
ATOM	2117	CA	GLY	274	8.713	46.269	-13.268	0.00	0.00	6
ATOM	2118	C	GLY	274	9.830	45.462	-13.913	0.00	0.00	6

Figure 23.14

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ATOM	2119	O	GLY	274	9.643	44.975	-15.019	0.00	0.00	8
ATOM	2120	N	ASN	275	10.923	45.207	-13.198	0.00	0.00	7
ATOM	2121	CA	ASN	275	12.031	44.497	-13.795	0.00	0.00	6
ATOM	2122	CB	ASN	275	13.296	45.296	-13.626	0.00	0.00	6
ATOM	2123	CG	ASN	275	13.164	46.690	-14.162	0.00	0.00	6
ATOM	2124	OD1	ASN	275	12.778	46.902	-15.309	0.00	0.00	8
ATOM	2125	ND2	ASN	275	13.461	47.664	-13.319	0.00	0.00	7
ATOM	2126	C	ASN	275	12.327	43.048	-13.447	0.00	0.00	6
ATOM	2127	O	ASN	275	13.267	42.486	-14.001	0.00	0.00	8
ATOM	2128	N	ILE	276	11.584	42.434	-12.531	0.00	0.00	7
ATOM	2129	CA	ILE	276	11.866	41.036	-12.189	0.00	0.00	6
ATOM	2130	CB	ILE	276	12.317	40.809	-10.687	0.00	0.00	6
ATOM	2131	CG2	ILE	276	13.643	41.508	-10.400	0.00	0.00	6
ATOM	2132	CG1	ILE	276	11.238	41.267	-9.707	0.00	0.00	6
ATOM	2133	CD1	ILE	276	11.518	40.911	-8.245	0.00	0.00	6
ATOM	2134	C	ILE	276	10.665	40.170	-12.511	0.00	0.00	6
ATOM	2135	O	ILE	276	9.538	40.653	-12.467	0.00	0.00	8
ATOM	2136	N	PHE	277	10.922	38.906	-12.864	0.00	0.00	7
ATOM	2137	CA	PHE	277	9.879	37.931	-13.204	0.00	0.00	6
ATOM	2138	CB	PHE	277	9.151	37.436	-11.942	0.00	0.00	6
ATOM	2139	CG	PHE	277	10.048	36.692	-10.993	0.00	0.00	6
ATOM	2140	CD1	PHE	277	10.279	37.179	-9.702	0.00	0.00	6
ATOM	2141	CD2	PHE	277	10.728	35.559	-11.418	0.00	0.00	6
ATOM	2142	CE1	PHE	277	11.186	36.548	-8.852	0.00	0.00	6
ATOM	2143	CE2	PHE	277	11.631	34.921	-10.582	0.00	0.00	6
ATOM	2144	CZ	PHE	277	11.867	35.416	-9.293	0.00	0.00	6
ATOM	2145	C	PHE	277	8.901	38.441	-14.243	0.00	0.00	6
ATOM	2146	O	PHE	277	7.708	38.176	-14.161	0.00	0.00	8
ATOM	2147	N	THR	278	9.442	39.166	-15.226	0.00	0.00	7
ATOM	2148	CA	THR	278	8.675	39.768	-16.329	0.00	0.00	6
ATOM	2149	CB	THR	278	9.578	40.666	-17.194	0.00	0.00	6
ATOM	2150	OG1	THR	278	10.712	39.911	-17.634	0.00	0.00	8
ATOM	2151	CG2	THR	278	10.074	41.888	-16.402	0.00	0.00	6
ATOM	2152	C	THR	278	7.972	38.737	-17.243	0.00	0.00	6
ATOM	2153	O	THR	278	7.034	39.085	-17.974	0.00	0.00	8
ATOM	2154	N	ARG	279	8.417	37.479	-17.190	0.00	0.00	7
ATOM	2155	CA	ARG	279	7.806	36.427	-17.993	0.00	0.00	6
ATOM	2156	CB	ARG	279	8.866	35.601	-18.722	0.00	0.00	6
ATOM	2157	CG	ARG	279	9.494	36.345	-19.885	0.00	0.00	6
ATOM	2158	CD	ARG	279	8.441	36.813	-20.862	0.00	0.00	6
ATOM	2159	NE	ARG	279	8.996	37.816	-21.751	0.00	0.00	7
ATOM	2160	CZ	ARG	279	8.445	39.006	-21.991	0.00	0.00	6
ATOM	2161	NH1	ARG	279	7.298	39.359	-21.411	0.00	0.00	7
ATOM	2162	NH2	ARG	279	9.071	39.868	-22.783	0.00	0.00	7
ATOM	2163	C	ARG	279	6.786	35.544	-17.273	0.00	0.00	6
ATOM	2164	O	ARG	279	6.447	34.465	-17.746	0.00	0.00	8
ATOM	2165	N	LEU	280	6.281	36.025	-16.142	0.00	0.00	7
ATOM	2166	CA	LEU	280	5.255	35.316	-15.377	0.00	0.00	6
ATOM	2167	CB	LEU	280	5.489	35.460	-13.865	0.00	0.00	6
ATOM	2168	CG	LEU	280	6.707	34.768	-13.261	0.00	0.00	6
ATOM	2169	CD1	LEU	280	6.719	35.031	-11.789	0.00	0.00	6
ATOM	2170	CD2	LEU	280	6.660	33.273	-13.532	0.00	0.00	6
ATOM	2171	C	LEU	280	3.966	35.998	-15.784	0.00	0.00	6
ATOM	2172	O	LEU	280	4.011	37.021	-16.462	0.00	0.00	8
ATOM	2173	N	PRO	281	2.797	35.448	-15.407	0.00	0.00	7
ATOM	2174	CD	PRO	281	2.533	34.197	-14.683	0.00	0.00	6
ATOM	2175	CA	PRO	281	1.538	36.091	-15.788	0.00	0.00	6
ATOM	2176	CB	PRO	281	0.494	35.250	-15.076	0.00	0.00	6
ATOM	2177	CG	PRO	281	1.112	33.894	-15.107	0.00	0.00	6
ATOM	2178	C	PRO	281	1.508	37.523	-15.301	0.00	0.00	6

Figure 23.15

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ATOM	2179	O	PRO	281	2.003	37.825	-14.214	0.00	0.00	8
ATOM	2180	N	LEU	282	0.935	38.386	-16.139	0.00	0.00	7
ATOM	2181	CA	LEU	282	0.803	39.818	-15.906	0.00	0.00	6
ATOM	2182	CB	LEU	282	-0.253	40.380	-16.862	0.00	0.00	6
ATOM	2183	CG	LEU	282	-0.631	41.845	-16.721	0.00	0.00	6
ATOM	2184	CD1	LEU	282	0.574	42.689	-16.995	0.00	0.00	6
ATOM	2185	CD2	LEU	282	-1.719	42.162	-17.691	0.00	0.00	6
ATOM	2186	C	LEU	282	0.398	40.150	-14.486	0.00	0.00	6
ATOM	2187	O	LEU	282	-0.581	39.608	-13.971	0.00	0.00	8
ATOM	2188	N	ALA	283	1.167	41.032	-13.857	0.00	0.00	7
ATOM	2189	CA	ALA	283	0.867	41.482	-12.503	0.00	0.00	6
ATOM	2190	CB	ALA	283	1.496	40.554	-11.459	0.00	0.00	6
ATOM	2191	C	ALA	283	1.391	42.908	-12.340	0.00	0.00	6
ATOM	2192	O	ALA	283	2.578	43.165	-12.503	0.00	0.00	8
ATOM	2193	N	ARG	284	0.492	43.836	-12.041	0.00	0.00	7
ATOM	2194	CA	ARG	284	0.871	45.224	-11.857	0.00	0.00	6
ATOM	2195	CB	ARG	284	0.221	46.106	-12.931	0.00	0.00	6
ATOM	2196	CG	ARG	284	0.543	45.713	-14.364	0.00	0.00	6
ATOM	2197	CD	ARG	284	1.989	46.015	-14.683	0.00	0.00	6
ATOM	2198	NE	ARG	284	2.326	45.745	-16.074	0.00	0.00	7
ATOM	2199	CZ	ARG	284	3.559	45.493	-16.497	0.00	0.00	6
ATOM	2200	NH1	ARG	284	4.578	45.465	-15.643	0.00	0.00	7
ATOM	2201	NH2	ARG	284	3.786	45.297	-17.781	0.00	0.00	7
ATOM	2202	C	ARG	284	0.338	45.627	-10.497	0.00	0.00	6
ATOM	2203	O	ARG	284	-0.867	45.520	-10.225	0.00	0.00	8
ATOM	2204	N	MET	285	1.237	46.089	-9.643	0.00	0.00	7
ATOM	2205	CA	MET	285	0.847	46.529	-8.308	0.00	0.00	6
ATOM	2206	CB	MET	285	2.087	46.868	-7.469	0.00	0.00	6
ATOM	2207	CG	MET	285	2.904	45.652	-7.037	0.00	0.00	6
ATOM	2208	SD	MET	285	1.890	44.362	-6.271	0.00	0.00	16
ATOM	2209	CE	MET	285	1.602	45.101	-4.693	0.00	0.00	6
ATOM	2210	C	MET	285	-0.123	47.722	-8.341	0.00	0.00	6
ATOM	2211	O	MET	285	-1.108	47.753	-7.594	0.00	0.00	8
ATOM	2212	N	TRP	286	0.123	48.676	-9.238	0.00	0.00	7
ATOM	2213	CA	TRP	286	-0.742	49.846	-9.313	0.00	0.00	6
ATOM	2214	CB	TRP	286	-0.219	50.882	-10.323	0.00	0.00	6
ATOM	2215	CG	TRP	286	-0.431	50.530	-11.769	0.00	0.00	6
ATOM	2216	CD2	TRP	286	-1.598	50.813	-12.556	0.00	0.00	6
ATOM	2217	CE2	TRP	286	-1.347	50.335	-13.869	0.00	0.00	6
ATOM	2218	CE3	TRP	286	-2.831	51.424	-12.282	0.00	0.00	6
ATOM	2219	CD1	TRP	286	0.461	49.900	-12.617	0.00	0.00	6
ATOM	2220	NE1	TRP	286	-0.090	49.784	-13.876	0.00	0.00	7
ATOM	2221	CZ2	TRP	286	-2.293	50.457	-14.907	0.00	0.00	6
ATOM	2222	CZ3	TRP	286	-3.772	51.538	-13.308	0.00	0.00	6
ATOM	2223	CH2	TRP	286	-3.494	51.057	-14.606	0.00	0.00	6
ATOM	2224	C	TRP	286	-2.192	49.488	-9.612	0.00	0.00	6
ATOM	2225	O	TRP	286	-3.085	50.273	-9.292	0.00	0.00	8
ATOM	2226	N	HIS	287	-2.441	48.309	-10.188	0.00	0.00	7
ATOM	2227	CA	HIS	287	-3.811	47.900	-10.509	0.00	0.00	6
ATOM	2228	CB	HIS	287	-3.834	46.532	-11.209	0.00	0.00	6
ATOM	2229	CG	HIS	287	-3.407	46.561	-12.647	0.00	0.00	6
ATOM	2230	CD2	HIS	287	-3.198	47.590	-13.506	0.00	0.00	6
ATOM	2231	ND1	HIS	287	-3.106	45.416	-13.353	0.00	0.00	7
ATOM	2232	CE1	HIS	287	-2.718	45.738	-14.575	0.00	0.00	6
ATOM	2233	NE2	HIS	287	-2.767	47.050	-14.693	0.00	0.00	7
ATOM	2234	C	HIS	287	-4.650	47.811	-9.234	0.00	0.00	6
ATOM	2235	O	HIS	287	-5.878	47.944	-9.264	0.00	0.00	8
ATOM	2236	N	GLN	288	-3.967	47.577	-8.117	0.00	0.00	7
ATOM	2237	CA	GLN	288	-4.610	47.443	-6.802	0.00	0.00	6
ATOM	2238	CB	GLN	288	-3.701	46.642	-5.862	0.00	0.00	6

Figure 23.16

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ATOM	2239	CG	GLN	288	-3.478	45.210	-6.320	0.00	0.00	6
ATOM	2240	CD	GLN	288	-2.388	44.516	-5.543	0.00	0.00	6
ATOM	2241	OE1	GLN	288	-1.497	43.898	-6.132	0.00	0.00	8
ATOM	2242	NE2	GLN	288	-2.434	44.622	-4.214	0.00	0.00	7
ATOM	2243	C	GLN	288	-4.978	48.777	-6.157	0.00	0.00	6
ATOM	2244	O	GLN	288	-5.824	48.838	-5.266	0.00	0.00	9
=====	=====	=====	=====	=====	=====	=====	=====	=====	=====	=====
ATOM	2283	N	GLY	294	-8.616	62.996	-7.864	0.00	0.00	7
ATOM	2284	CA	GLY	294	-7.718	64.021	-7.349	0.00	0.00	6
ATOM	2285	C	GLY	294	-6.522	63.501	-6.557	0.00	0.00	6
ATOM	2286	O	GLY	294	-5.796	64.272	-5.930	0.00	0.00	8
ATOM	2287	N	ASP	295	-6.368	62.187	-6.508	0.00	0.00	7
ATOM	2288	CA	ASP	295	-5.239	61.593	-5.828	0.00	0.00	6
ATOM	2289	CB	ASP	295	-5.606	60.232	-5.239	0.00	0.00	6
ATOM	2290	CG	ASP	295	-6.281	60.339	-3.884	0.00	0.00	6
ATOM	2291	OD1	ASP	295	-6.508	61.465	-3.386	0.00	0.00	8
ATOM	2292	OD2	ASP	295	-6.583	59.269	-3.313	0.00	0.00	8
ATOM	2293	C	ASP	295	-4.219	61.398	-6.918	0.00	0.00	6
ATOM	2294	O	ASP	295	-4.566	61.211	-8.084	0.00	0.00	8
ATOM	2295	N	ALA	296	-2.956	61.491	-6.558	0.00	0.00	7
ATOM	2296	CA	ALA	296	-1.899	61.296	-7.521	0.00	0.00	6
ATOM	2297	CB	ALA	296	-0.972	62.464	-7.509	0.00	0.00	6
ATOM	2298	C	ALA	296	-1.148	60.046	-7.129	0.00	0.00	6
ATOM	2299	O	ALA	296	-1.077	59.684	-5.944	0.00	0.00	8
ATOM	2300	N	VAL	297	-0.606	59.377	-8.134	0.00	0.00	7
ATOM	2301	CA	VAL	297	0.168	58.178	-7.907	0.00	0.00	6
ATOM	2302	CB	VAL	297	-0.226	57.053	-8.891	0.00	0.00	6
ATOM	2303	CG1	VAL	297	0.648	55.834	-8.686	0.00	0.00	6
ATOM	2304	CG2	VAL	297	-1.655	56.686	-8.709	0.00	0.00	6
ATOM	2305	C	VAL	297	1.618	58.558	-8.157	0.00	0.00	6
ATOM	2306	O	VAL	297	1.938	59.111	-9.233	0.00	0.00	8
ATOM	2307	N	ARG	298	2.466	58.375	-7.140	0.00	0.00	7
ATOM	2308	CA	ARG	298	3.887	58.647	-7.278	0.00	0.00	6
ATOM	2309	CB	ARG	298	4.404	59.591	-6.203	0.00	0.00	6
ATOM	2310	CG	ARG	298	5.916	59.827	-6.337	0.00	0.00	6
ATOM	2311	CD	ARG	298	6.491	60.782	-5.309	0.00	0.00	6
ATOM	2312	NE	ARG	298	6.961	60.120	-4.094	0.00	0.00	7
ATOM	2313	CZ	ARG	298	6.335	60.172	-2.919	0.00	0.00	6
ATOM	2314	NH1	ARG	298	5.207	60.866	-2.796	0.00	0.00	7
ATOM	2315	NH2	ARG	298	6.818	59.505	-1.870	0.00	0.00	7
ATOM	2316	C	ARG	298	4.601	57.304	-7.153	0.00	0.00	6
ATOM	2317	O	ARG	298	4.235	56.488	-6.312	0.00	0.00	8
ATOM	2318	N	MET	299	5.615	57.074	-7.975	0.00	0.00	7
ATOM	2319	CA	MET	299	6.350	55.831	-7.920	0.00	0.00	6
ATOM	2320	CB	MET	299	6.558	55.267	-9.327	0.00	0.00	6
ATOM	2321	CG	MET	299	7.262	53.919	-9.359	0.00	0.00	6
ATOM	2322	SD	MET	299	7.645	53.364	-11.007	0.00	0.00	16
ATOM	2323	CE	MET	299	9.150	54.215	-11.342	0.00	0.00	6
ATOM	2324	C	MET	299	7.703	56.079	-7.290	0.00	0.00	6
ATOM	2325	O	MET	299	8.433	56.971	-7.733	0.00	0.00	8
ATOM	2326	N	ASP	300	8.056	55.275	-6.290	0.00	0.00	7
ATOM	2327	CA	ASP	300	9.343	55.404	-5.613	0.00	0.00	6
ATOM	2328	CB	ASP	300	9.158	55.690	-4.126	0.00	0.00	6
ATOM	2329	CG	ASP	300	8.716	57.098	-3.835	0.00	0.00	6
ATOM	2330	OD1	ASP	300	8.569	57.929	-4.760	0.00	0.00	8
ATOM	2331	OD2	ASP	300	8.502	57.364	-2.642	0.00	0.00	8
ATOM	2332	C	ASP	300	10.068	54.086	-5.687	0.00	0.00	6
ATOM	2333	O	ASP	300	9.455	53.051	-5.864	0.00	0.00	8
ATOM	2334	N	PRO	301	11.394	54.108	-5.534	0.00	0.00	7
ATOM	2335	CD	PRO	301	12.291	55.278	-5.447	0.00	0.00	6

Figure 23.17

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ATOM	2336	CA	PRO	301	12.145	52.849	-5.568	0.00	0.00	6
ATOM	2337	CB	PRO	301	13.584	53.315	-5.385	0.00	0.00	6
ATOM	2338	CG	PRO	301	13.563	54.734	-5.991	0.00	0.00	6
ATOM	2339	C	PRO	301	11.672	51.992	-4.371	0.00	0.00	6
ATOM	2340	O	PRO	301	11.280	52.520	-3.319	0.00	0.00	8
ATOM	2341	N	PRO	302	11.703	50.671	-4.507	0.00	0.00	7
ATOM	2342	CD	PRO	302	12.233	49.843	-5.589	0.00	0.00	6
ATOM	2343	CA	PRO	302	11.259	49.818	-3.412	0.00	0.00	5
ATOM	2344	CB	PRO	302	11.429	48.427	-4.005	0.00	0.00	6
ATOM	2345	CG	PRO	302	12.588	48.584	-4.852	0.00	0.00	6
ATOM	2346	C	PRO	302	12.022	49.981	-2.103	0.00	0.00	5
ATOM	2347	O	PRO	302	13.262	50.022	-2.084	0.00	0.00	8
ATOM	2348	N	CYS	303	11.250	50.124	-1.022	0.00	0.00	7
ATOM	2349	CA	CYS	303	11.781	50.260	0.334	0.00	0.00	6
ATOM	2350	C	CYS	303	12.739	51.391	0.542	0.00	0.00	6
ATOM	2351	O	CYS	303	13.597	51.309	1.404	0.00	0.00	8
ATOM	2352	CB	CYS	303	12.453	48.965	0.797	0.00	0.00	6
ATOM	2353	SG	CYS	303	11.287	47.610	1.151	0.00	0.00	16
ATOM	2354	N	THR	304	12.602	52.440	-0.264	0.00	0.00	7
ATOM	2355	CA	THR	304	13.447	53.618	-0.167	0.00	0.00	6
ATOM	2356	CB	THR	304	14.140	53.967	-1.499	0.00	0.00	6
ATOM	2357	OG1	THR	304	13.162	54.438	-2.432	0.00	0.00	8
ATOM	2358	CG2	THR	304	14.859	52.765	-2.070	0.00	0.00	6
ATOM	2359	C	THR	304	12.571	54.792	0.243	0.00	0.00	6
ATOM	2360	O	THR	304	11.354	54.802	0.008	0.00	0.00	8
ATOM	2361	N	ASN	305	13.210	55.764	0.878	0.00	0.00	7
ATOM	2362	CA	ASN	305	12.552	56.962	1.334	0.00	0.00	6
ATOM	2363	CB	ASN	305	12.859	57.170	2.814	0.00	0.00	6
ATOM	2364	CG	ASN	305	12.016	58.235	3.414	0.00	0.00	6
ATOM	2365	OD1	ASN	305	11.397	59.008	2.692	0.00	0.00	8
ATOM	2366	ND2	ASN	305	11.963	58.295	4.733	0.00	0.00	7
ATOM	2367	C	ASN	305	13.159	58.079	0.487	0.00	0.00	6
ATOM	2368	O	ASN	305	14.365	58.272	0.509	0.00	0.00	8
ATOM	2369	N	THR	306	12.341	58.782	-0.293	0.00	0.00	7
ATOM	2370	CA	THR	306	12.859	59.841	-1.151	0.00	0.00	6
ATOM	2371	CB	THR	306	12.269	59.700	-2.555	0.00	0.00	6
ATOM	2372	OG1	THR	306	10.835	59.751	-2.473	0.00	0.00	8
ATOM	2373	CG2	THR	306	12.722	58.357	-3.180	0.00	0.00	6
ATOM	2374	C	THR	306	12.662	61.272	-0.628	0.00	0.00	6
ATOM	2375	O	THR	306	13.099	62.243	-1.244	0.00	0.00	8
ATOM	2376	N	THR	307	12.058	61.382	0.542	0.00	0.00	7
ATOM	2377	CA	THR	307	11.796	62.662	1.166	0.00	0.00	6
ATOM	2378	CB	THR	307	11.210	62.436	2.554	0.00	0.00	6
ATOM	2379	OG1	THR	307	10.097	61.536	2.456	0.00	0.00	8
ATOM	2380	CG2	THR	307	10.778	63.768	3.181	0.00	0.00	6
ATOM	2381	C	THR	307	12.971	63.629	1.295	0.00	0.00	6
ATOM	2382	O	THR	307	12.829	64.792	0.982	0.00	0.00	8
ATOM	2383	N	ALA	308	14.125	63.186	1.772	0.00	0.00	7
ATOM	2384	CA	ALA	308	15.238	64.114	1.930	0.00	0.00	6
ATOM	2385	CB	ALA	308	16.418	63.443	2.620	0.00	0.00	6
ATOM	2386	C	ALA	308	15.677	64.725	0.604	0.00	0.00	6
ATOM	2387	O	ALA	308	15.855	65.931	0.504	0.00	0.00	8
ATOM	2388	N	ALA	309	15.821	63.894	-0.422	0.00	0.00	7
ATOM	2389	CA	ALA	309	16.253	64.367	-1.734	0.00	0.00	6
ATOM	2390	CB	ALA	309	16.610	63.166	-2.613	0.00	0.00	6
ATOM	2391	C	ALA	309	15.194	65.247	-2.420	0.00	0.00	6
ATOM	2392	O	ALA	309	15.485	66.306	-2.963	0.00	0.00	8
=====	=====	=====	=====	=====	=====	=====	=====	=====	=====	=====
ATOM	2529	N	GLN	327	8.486	76.823	-14.820	0.00	0.00	7
ATOM	2530	CA	GLN	327	7.270	76.141	-15.206	0.00	0.00	5

Figure 23.18

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ATOM	2531	CB	GLN	327	6.891	76.509	-16.641	0.00	0.00	6
ATOM	2532	CG	GLN	327	7.559	75.650	-17.725	0.00	0.00	6
ATOM	2533	CD	GLN	327	8.914	76.160	-18.181	0.00	0.00	6
ATOM	2534	OE1	GLN	327	9.580	75.503	-18.991	0.00	0.00	8
ATOM	2535	NE2	GLN	327	9.326	77.335	-17.684	0.00	0.00	7
ATOM	2536	C	GLN	327	7.326	74.624	-15.044	0.00	0.00	6
ATOM	2537	O	GLN	327	6.289	73.955	-15.084	0.00	0.00	8
ATOM	2538	N	LEU	328	8.525	74.080	-14.861	0.00	0.00	7
ATOM	2539	CA	LEU	328	8.679	72.642	-14.728	0.00	0.00	6
ATOM	2540	CB	LEU	328	10.159	72.240	-14.772	0.00	0.00	6
ATOM	2541	CG	LEU	328	10.805	72.604	-16.108	0.00	0.00	6
ATOM	2542	CD1	LEU	328	12.081	71.896	-16.233	0.00	0.00	6
ATOM	2543	CD2	LEU	328	9.906	72.211	-17.256	0.00	0.00	6
ATOM	2544	C	LEU	328	8.001	72.104	-13.487	0.00	0.00	6
ATOM	2545	O	LEU	328	7.967	72.758	-12.449	0.00	0.00	8
ATOM	2546	N	PRO	329	7.402	70.902	-13.593	0.00	0.00	7
ATOM	2547	CD	PRO	329	7.290	70.086	-14.813	0.00	0.00	6
ATOM	2548	CA	PRO	329	6.705	70.251	-12.477	0.00	0.00	6
ATOM	2549	CB	PRO	329	6.110	68.992	-13.115	0.00	0.00	6
ATOM	2550	CG	PRO	329	6.016	69.344	-14.565	0.00	0.00	6
ATOM	2551	C	PRO	329	7.673	69.894	-11.351	0.00	0.00	6
ATOM	2552	O	PRO	329	8.902	69.995	-11.480	0.00	0.00	8
ATOM	2553	N	GLN	330	7.093	69.415	-10.264	0.00	0.00	7
ATOM	2554	CA	GLN	330	7.835	69.066	-9.071	0.00	0.00	6
ATOM	2555	CB	GLN	330	6.808	68.680	-8.004	0.00	0.00	6
ATOM	2556	CG	GLN	330	7.319	67.845	-6.870	0.00	0.00	6
ATOM	2557	CD	GLN	330	6.188	67.187	-6.123	0.00	0.00	6
ATOM	2558	OE1	GLN	330	5.065	67.674	-6.135	0.00	0.00	8
ATOM	2559	NE2	GLN	330	6.471	66.055	-5.491	0.00	0.00	7
ATOM	2560	C	GLN	330	8.810	67.932	-9.348	0.00	0.00	6
ATOM	2561	O	GLN	330	8.546	67.069	-10.186	0.00	0.00	8
ATOM	2562	N	TRP	331	9.958	67.960	-8.686	0.00	0.00	7
ATOM	2563	CA	TRP	331	10.914	66.901	-8.848	0.00	0.00	6
ATOM	2564	CB	TRP	331	12.297	67.359	-8.387	0.00	0.00	6
ATOM	2565	CG	TRP	331	13.395	66.349	-8.625	0.00	0.00	6
ATOM	2566	CD2	TRP	331	13.827	65.291	-7.729	0.00	0.00	6
ATOM	2567	CE2	TRP	331	14.870	64.602	-8.374	0.00	0.00	6
ATOM	2568	CE3	TRP	331	13.429	64.870	-6.442	0.00	0.00	6
ATOM	2569	CD1	TRP	331	14.183	66.253	-9.729	0.00	0.00	6
ATOM	2570	NE1	TRP	331	15.071	65.215	-9.585	0.00	0.00	7
ATOM	2571	CZ2	TRP	331	15.537	63.504	-7.783	0.00	0.00	6
ATOM	2572	CZ3	TRP	331	14.091	63.776	-5.852	0.00	0.00	6
ATOM	2573	CH2	TRP	331	15.136	63.112	-6.527	0.00	0.00	6
ATOM	2574	C	TRP	331	10.466	65.684	-8.018	0.00	0.00	6
ATOM	2575	O	TRP	331	9.923	65.818	-6.917	0.00	0.00	8
ATOM	2576	N	ASP	332	10.642	64.501	-8.603	0.00	0.00	7
ATOM	2577	CA	ASP	332	10.349	63.200	-7.969	0.00	0.00	6
ATOM	2578	CB	ASP	332	9.084	62.538	-8.515	0.00	0.00	6
ATOM	2579	CG	ASP	332	7.858	63.322	-8.214	0.00	0.00	6
ATOM	2580	OD1	ASP	332	7.767	63.875	-7.097	0.00	0.00	8
ATOM	2581	OD2	ASP	332	6.984	63.367	-9.102	0.00	0.00	8
ATOM	2582	C	ASP	332	11.527	62.334	-8.349	0.00	0.00	6
ATOM	2583	O	ASP	332	12.108	62.512	-9.424	0.00	0.00	8
ATOM	2584	N	MET	333	11.921	61.416	-7.487	0.00	0.00	7
ATOM	2585	CA	MET	333	13.049	60.609	-7.887	0.00	0.00	6
ATOM	2586	CB	MET	333	13.614	59.802	-6.735	0.00	0.00	6
ATOM	2587	CG	MET	333	15.038	59.439	-7.018	0.00	0.00	6
ATOM	2588	SD	MET	333	15.679	58.885	-5.560	0.00	0.00	16
ATOM	2589	CE	MET	333	16.287	60.400	-4.882	0.00	0.00	6
ATOM	2590	C	MET	333	12.753	59.701	-9.079	0.00	0.00	6

Figure 23.19

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ATOM	2591	O	MET	333	13.665	59.342	-9.815	0.00	0.00	8
ATOM	2592	N	CYS	334	11.478	59.371	-9.270	0.00	0.00	7
ATOM	2593	CA	CYS	334	11.026	58.513	-10.367	0.00	0.00	6
ATOM	2594	C	CYS	334	9.702	59.029	-10.916	0.00	0.00	6
ATOM	2595	O	CYS	334	8.888	59.635	-10.198	0.00	0.00	8
ATOM	2596	CB	CYS	334	10.815	57.047	-9.897	0.00	0.00	6
ATOM	2597	SG	CYS	334	12.242	56.207	-9.148	0.00	0.00	16
ATOM	2598	N	ASN	335	9.486	58.803	-12.204	0.00	0.00	7
ATOM	2599	CA	ASN	335	8.235	59.224	-12.824	0.00	0.00	6
ATOM	2600	CB	ASN	335	8.492	60.030	-14.089	0.00	0.00	6
ATOM	2601	CG	ASN	335	7.263	60.696	-14.577	0.00	0.00	6
ATOM	2602	OD1	ASN	335	6.359	60.059	-15.081	0.00	0.00	8
ATOM	2603	ND2	ASN	335	7.178	61.978	-14.345	0.00	0.00	7
ATOM	2604	C	ASN	335	7.397	57.993	-13.146	0.00	0.00	6
ATOM	2605	O	ASN	335	7.763	57.217	-14.032	0.00	0.00	8
ATOM	2606	N	PHE	336	6.307	57.804	-12.394	0.00	0.00	7
ATOM	2607	CA	PHE	336	5.405	56.674	-12.567	0.00	0.00	6
ATOM	2608	CB	PHE	336	4.208	56.808	-11.619	0.00	0.00	6
ATOM	2609	CG	PHE	336	3.161	55.748	-11.809	0.00	0.00	6
ATOM	2610	CD1	PHE	336	3.345	54.470	-11.308	0.00	0.00	6
ATOM	2611	CD2	PHE	336	2.011	56.015	-12.539	0.00	0.00	6
ATOM	2612	CE1	PHE	336	2.397	53.474	-11.544	0.00	0.00	6
ATOM	2613	CE2	PHE	336	1.067	55.029	-12.777	0.00	0.00	6
ATOM	2614	CZ	PHE	336	1.260	53.763	-12.281	0.00	0.00	6
ATOM	2615	C	PHE	336	4.928	56.535	-14.011	0.00	0.00	6
ATOM	2616	O	PHE	336	5.014	55.454	-14.590	0.00	0.00	8
ATOM	2617	N	LEU	337	4.433	57.630	-14.585	0.00	0.00	7
ATOM	2618	CA	LEU	337	3.948	57.636	-15.966	0.00	0.00	6
ATOM	2619	CB	LEU	337	3.300	58.989	-16.304	0.00	0.00	6
ATOM	2620	CG	LEU	337	1.946	59.230	-15.616	0.00	0.00	6
ATOM	2621	CD1	LEU	337	1.284	60.481	-16.148	0.00	0.00	6
ATOM	2622	CD2	LEU	337	1.015	58.057	-15.853	0.00	0.00	6
ATOM	2623	C	LEU	337	5.036	57.253	-16.989	0.00	0.00	6
ATOM	2624	O	LEU	337	4.754	56.576	-17.951	0.00	0.00	8
ATOM	2625	N	VAL	338	6.270	57.679	-16.780	0.00	0.00	7
ATOM	2626	CA	VAL	338	7.348	57.311	-17.693	0.00	0.00	6
ATOM	2627	CB	VAL	338	8.639	58.100	-17.378	0.00	0.00	6
ATOM	2628	CG1	VAL	338	9.872	57.392	-17.931	0.00	0.00	6
ATOM	2629	CG2	VAL	338	8.537	59.510	-17.943	0.00	0.00	6
ATOM	2630	C	VAL	338	7.628	55.793	-17.618	0.00	0.00	6
ATOM	2631	O	VAL	338	7.734	55.110	-18.645	0.00	0.00	8
ATOM	2632	N	ASN	339	7.756	55.272	-16.395	0.00	0.00	7
ATOM	2633	CA	ASN	339	8.008	53.847	-16.185	0.00	0.00	6
ATOM	2634	CB	ASN	339	8.241	53.573	-14.697	0.00	0.00	6
ATOM	2635	CG	ASN	339	8.321	52.086	-14.373	0.00	0.00	6
ATOM	2636	OD1	ASN	339	7.302	51.421	-14.241	0.00	0.00	8
ATOM	2637	ND2	ASN	339	9.517	51.581	-14.206	0.00	0.00	7
ATOM	2638	C	ASN	339	6.815	53.041	-16.721	0.00	0.00	6
ATOM	2639	O	ASN	339	6.996	51.990	-17.343	0.00	0.00	8
ATOM	2640	N	LEU	340	5.608	53.559	-16.514	0.00	0.00	7
ATOM	2641	CA	LEU	340	4.380	52.922	-16.983	0.00	0.00	6
ATOM	2642	CB	LEU	340	3.163	53.742	-16.516	0.00	0.00	6
ATOM	2643	CG	LEU	340	1.738	53.386	-16.972	0.00	0.00	6
ATOM	2644	CD1	LEU	340	1.170	52.220	-16.186	0.00	0.00	6
ATOM	2645	CD2	LEU	340	0.859	54.570	-16.748	0.00	0.00	6
ATOM	2646	C	LEU	340	4.264	52.726	-18.514	0.00	0.00	6
ATOM	2647	O	LEU	340	3.728	51.712	-18.984	0.00	0.00	8
ATOM	2648	N	GLN	341	4.729	53.714	-19.281	0.00	0.00	7
ATOM	2649	CA	GLN	341	4.616	53.709	-20.741	0.00	0.00	6
ATOM	2650	CB	GLN	341	4.306	55.106	-21.232	0.00	0.00	6

Figure 23.20

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ATOM	2651	CG	GLN	341	3.049	55.688	-20.671	0.00	0.00	6
ATOM	2652	CD	GLN	341	2.919	57.129	-21.056	0.00	0.00	6
ATOM	2653	OE1	GLN	341	3.636	57.980	-20.536	0.00	0.00	8
ATOM	2654	NE2	GLN	341	2.064	57.412	-22.036	0.00	0.00	7
ATOM	2655	C	GLN	341	5.868	53.271	-21.407	0.00	0.00	6
ATOM	2656	O	GLN	341	5.967	53.290	-22.637	0.00	0.00	8
ATOM	2657	N	TYR	342	6.840	52.918	-20.586	0.00	0.00	7
ATOM	2658	CA	TYR	342	8.132	52.492	-21.068	0.00	0.00	6
ATOM	2659	CB	TYR	342	9.163	52.533	-19.929	0.00	0.00	6
ATOM	2660	CG	TYR	342	10.586	52.464	-20.404	0.00	0.00	6
ATOM	2661	CD1	TYR	342	11.278	53.628	-20.702	0.00	0.00	6
ATOM	2662	CE1	TYR	342	12.557	53.586	-21.194	0.00	0.00	6
ATOM	2663	CD2	TYR	342	11.215	51.249	-20.619	0.00	0.00	6
ATOM	2664	CE2	TYR	342	12.500	51.200	-21.121	0.00	0.00	6
ATOM	2665	CZ	TYR	342	13.156	52.378	-21.413	0.00	0.00	6
ATOM	2666	OH	TYR	342	14.423	52.395	-21.943	0.00	0.00	8
ATOM	2667	C	TYR	342	8.085	51.099	-21.687	0.00	0.00	6
ATOM	2668	O	TYR	342	7.511	50.170	-21.113	0.00	0.00	8
ATOM	2669	N	ARG	343	8.705	50.985	-22.867	0.00	0.00	7
ATOM	2670	CA	ARG	343	8.786	49.742	-23.612	0.00	0.00	6
ATOM	2671	CB	ARG	343	8.255	49.912	-25.031	0.00	0.00	6
ATOM	2672	CG	ARG	343	6.815	50.370	-25.083	0.00	0.00	6
ATOM	2673	CD	ARG	343	5.858	49.437	-24.311	0.00	0.00	6
ATOM	2674	NE	ARG	343	4.527	50.043	-24.164	0.00	0.00	7
ATOM	2675	CZ	ARG	343	3.917	50.284	-23.003	0.00	0.00	6
ATOM	2676	NH1	ARG	343	4.483	49.951	-21.842	0.00	0.00	7
ATOM	2677	NH2	ARG	343	2.797	50.997	-23.001	0.00	0.00	7
ATOM	2678	C	ARG	343	10.200	49.210	-23.643	0.00	0.00	6
ATOM	2679	O	ARG	343	11.126	49.841	-24.174	0.00	0.00	8
ATOM	2680	N	ARG	344	10.345	48.050	-23.017	0.00	0.00	7
ATOM	2681	CA	ARG	344	11.602	47.344	-22.925	0.00	0.00	6
ATOM	2682	CB	ARG	344	11.554	46.402	-21.714	0.00	0.00	6
ATOM	2683	CG	ARG	344	11.203	47.131	-20.404	0.00	0.00	6
ATOM	2684	CD	ARG	344	11.156	46.157	-19.244	0.00	0.00	6
ATOM	2685	NE	ARG	344	11.224	46.784	-17.926	0.00	0.00	7
ATOM	2686	CZ	ARG	344	10.283	47.585	-17.455	0.00	0.00	6
ATOM	2687	NH1	ARG	344	9.233	47.849	-18.207	0.00	0.00	7
ATOM	2688	NH2	ARG	344	10.354	48.075	-16.221	0.00	0.00	7
ATOM	2689	C	ARG	344	11.731	46.579	-24.253	0.00	0.00	6
ATOM	2690	O	ARG	344	10.823	45.871	-24.657	0.00	0.00	8
ATOM	2691	N	LEU	345	12.834	46.779	-24.953	0.00	0.00	7
ATOM	2692	CA	LEU	345	13.022	46.146	-26.238	0.00	0.00	6
ATOM	2693	CB	LEU	345	13.413	47.193	-27.302	0.00	0.00	6
ATOM	2694	CG	LEU	345	12.566	48.468	-27.368	0.00	0.00	6
ATOM	2695	CD1	LEU	345	13.194	49.422	-28.350	0.00	0.00	6
ATOM	2696	CD2	LEU	345	11.127	48.192	-27.708	0.00	0.00	6
ATOM	2697	C	LEU	345	14.059	45.064	-26.148	0.00	0.00	6
ATOM	2698	O	LEU	345	13.855	44.001	-26.687	0.00	0.00	8
ATOM	2699	N	TYR	346	15.176	45.312	-25.475	0.00	0.00	7
ATOM	2700	CA	TYR	346	16.195	44.279	-25.365	0.00	0.00	6
ATOM	2701	CB	TYR	346	17.563	44.886	-25.225	0.00	0.00	6
ATOM	2702	CG	TYR	346	17.875	45.813	-26.336	0.00	0.00	6
ATOM	2703	CD1	TYR	346	17.509	47.151	-26.265	0.00	0.00	6
ATOM	2704	CE1	TYR	346	17.801	48.024	-27.293	0.00	0.00	6
ATOM	2705	CD2	TYR	346	18.541	45.364	-27.464	0.00	0.00	6
ATOM	2706	CE2	TYR	346	18.842	46.230	-28.498	0.00	0.00	6
ATOM	2707	CZ	TYR	346	18.472	47.564	-28.406	0.00	0.00	6
ATOM	2708	OH	TYR	346	18.816	48.451	-29.395	0.00	0.00	8
ATOM	2709	C	TYR	346	15.966	43.379	-24.176	0.00	0.00	6
ATOM	2710	O	TYR	346	15.682	43.851	-23.072	0.00	0.00	8

Figure 23.21

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ATOM	2711	N	ARG	347	16.170	42.088	-24.394	0.00	0.00	7
ATOM	2712	CA	ARG	347	15.997	41.087	-23.349	0.00	0.00	6
ATOM	2713	CB	ARG	347	15.299	39.857	-23.930	0.00	0.00	6
ATOM	2714	CG	ARG	347	13.824	40.092	-24.184	0.00	0.00	6
ATOM	2715	CD	ARG	347	13.029	39.837	-22.915	0.00	0.00	6
ATOM	2716	NE	ARG	347	12.346	41.018	-22.405	0.00	0.00	7
ATOM	2717	CZ	ARG	347	11.690	41.040	-21.250	0.00	0.00	6
ATOM	2718	NH1	ARG	347	11.636	39.942	-20.489	0.00	0.00	7
ATOM	2719	NH2	ARG	347	11.064	42.150	-20.672	0.00	0.00	7
ATOM	2720	C	ARG	347	17.355	40.705	-22.758	0.00	0.00	6
ATOM	2721	O	ARG	347	17.438	40.211	-21.637	0.00	0.00	8
ATOM	2722	N	SER	348	18.411	40.980	-23.510	0.00	0.00	7
ATOM	2723	CA	SER	348	19.768	40.667	-23.094	0.00	0.00	6
ATOM	2724	CB	SER	348	20.129	39.264	-23.611	0.00	0.00	6
ATOM	2725	OG	SER	348	21.509	39.005	-23.442	0.00	0.00	8
ATOM	2726	C	SER	348	20.727	41.700	-23.704	0.00	0.00	6
ATOM	2727	O	SER	348	20.426	42.262	-24.754	0.00	0.00	8
ATOM	2728	N	MET	349	21.876	41.916	-23.052	0.00	0.00	7
ATOM	2729	CA	MET	349	22.910	42.839	-23.522	0.00	0.00	6
ATOM	2730	CB	MET	349	23.375	43.751	-22.380	0.00	0.00	6
ATOM	2731	CG	MET	349	22.376	44.853	-21.983	0.00	0.00	6
ATOM	2732	SD	MET	349	22.063	46.109	-23.244	0.00	0.00	16
ATOM	2733	CE	MET	349	20.524	45.599	-23.844	0.00	0.00	6
ATOM	2734	C	MET	349	24.130	42.128	-24.122	0.00	0.00	6
ATOM	2735	O	MET	349	25.182	42.732	-24.298	0.00	0.00	8
ATOM	2736	N	ASN	350	23.974	40.854	-24.469	0.00	0.00	7
ATOM	2737	CA	ASN	350	25.068	40.066	-25.026	0.00	0.00	6
ATOM	2738	CB	ASN	350	24.620	38.629	-25.302	0.00	0.00	6
ATOM	2739	CG	ASN	350	24.814	37.700	-24.102	0.00	0.00	6
ATOM	2740	OD1	ASN	350	25.925	37.213	-23.845	0.00	0.00	8
ATOM	2741	ND2	ASN	350	23.724	37.422	-23.379	0.00	0.00	7
ATOM	2742	C	ASN	350	25.652	40.659	-26.293	0.00	0.00	6
ATOM	2743	O	ASN	350	26.880	40.737	-26.410	0.00	0.00	8
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ATOM	2871	N	LEU	366	31.679	45.222	-14.828	0.00	0.00	7
ATOM	2872	CA	LEU	366	30.314	45.021	-14.325	0.00	0.00	6
ATOM	2873	CB	LEU	366	29.564	43.843	-14.987	0.00	0.00	6
ATOM	2874	CG	LEU	366	28.817	44.056	-16.331	0.00	0.00	6
ATOM	2875	CD1	LEU	366	29.791	44.164	-17.487	0.00	0.00	6
ATOM	2876	CD2	LEU	366	27.880	42.910	-16.607	0.00	0.00	6
ATOM	2877	C	LEU	366	30.610	44.731	-12.845	0.00	0.00	6
ATOM	2878	O	LEU	366	31.409	43.857	-12.529	0.00	0.00	8
ATOM	2879	N	TYR	367	30.026	45.511	-11.940	0.00	0.00	7
ATOM	2880	CA	TYR	367	30.273	45.313	-10.505	0.00	0.00	6
ATOM	2881	CB	TYR	367	31.151	46.462	-9.960	0.00	0.00	6
ATOM	2882	CG	TYR	367	30.489	47.835	-10.015	0.00	0.00	6
ATOM	2883	CD1	TYR	367	29.581	48.221	-9.031	0.00	0.00	6
ATOM	2884	CE1	TYR	367	28.979	49.457	-9.065	0.00	0.00	6
ATOM	2885	CD2	TYR	367	30.775	48.746	-11.052	0.00	0.00	6
ATOM	2886	CE2	TYR	367	30.155	50.021	-11.103	0.00	0.00	6
ATOM	2887	CZ	TYR	367	29.257	50.370	-10.102	0.00	0.00	6
ATOM	2888	OH	TYR	367	28.634	51.610	-10.097	0.00	0.00	8
ATOM	2889	C	TYR	367	28.946	45.193	-9.755	0.00	0.00	6
ATOM	2890	O	TYR	367	28.015	45.963	-10.020	0.00	0.00	8
ATOM	2891	N	ASN	368	28.813	44.161	-8.920	0.00	0.00	7
ATOM	2892	CA	ASN	368	27.582	43.978	-8.159	0.00	0.00	6
ATOM	2893	CB	ASN	368	26.822	42.715	-8.584	0.00	0.00	6
ATOM	2894	CG	ASN	368	26.280	42.805	-9.977	0.00	0.00	6
ATOM	2895	OD1	ASN	368	27.037	42.925	-10.919	0.00	0.00	8
ATOM	2896	ND2	ASN	368	24.976	42.657	-10.126	0.00	0.00	7

Figure 23.22

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ATOM	2897	C	ASN	368	27.766	43.869	-6.640	0.00	0.00	6
ATOM	2898	O	ASN	368	28.737	43.286	-6.154	0.00	0.00	8
ATOM	2899	N	GLY	369	26.819	44.429	-5.900	0.00	0.00	7
ATOM	2900	CA	GLY	369	26.840	44.297	-4.463	0.00	0.00	6
ATOM	2901	C	GLY	369	26.143	42.956	-4.271	0.00	0.00	6.
ATOM	2902	O	GLY	369	25.030	42.750	-4.816	0.00	0.00	8
ATOM	2903	N	ASP	370	26.777	42.072	-3.497	0.00	0.00	7
ATOM	2904	CA	ASP	370	26.279	40.724	-3.247	0.00	0.00	6
ATOM	2905	CB	ASP	370	27.431	39.815	-2.852	0.00	0.00	6
ATOM	2906	CG	ASP	370	28.041	40.174	-1.506	0.00	0.00	6
ATOM	2907	OD1	ASP	370	27.461	40.971	-0.722	0.00	0.00	8
ATOM	2908	OD2	ASP	370	29.117	39.629	-1.242	0.00	0.00	8
ATOM	2909	C	ASP	370	25.083	40.467	-2.331	0.00	0.00	6
ATOM	2910	O	ASP	370	24.723	39.314	-2.105	0.00	0.00	8
ATOM	2911	N	VAL	371	24.463	41.509	-1.787	0.00	0.00	7
ATOM	2912	CA	VAL	371	23.286	41.296	-0.946	0.00	0.00	6
ATOM	2913	CB	VAL	371	23.473	41.749	0.535	0.00	0.00	6
ATOM	2914	CG1	VAL	371	24.644	41.016	1.129	0.00	0.00	6
ATOM	2915	CG2	VAL	371	23.657	43.245	0.652	0.00	0.00	6
ATOM	2916	C	VAL	371	22.070	41.919	-1.575	0.00	0.00	6
ATOM	2917	O	VAL	371	21.030	42.015	-0.948	0.00	0.00	8
ATOM	2918	N	ASP	372	22.217	42.318	-2.840	0.00	0.00	7
ATOM	2919	CA	ASP	372	21.128	42.895	-3.626	0.00	0.00	6
ATOM	2920	CB	ASP	372	21.699	43.804	-4.726	0.00	0.00	6
ATOM	2921	CG	ASP	372	20.643	44.258	-5.734	0.00	0.00	6
ATOM	2922	OD1	ASP	372	19.493	44.548	-5.349	0.00	0.00	8
ATOM	2923	OD2	ASP	372	20.983	44.338	-6.927	0.00	0.00	8
ATOM	2924	C	ASP	372	20.328	41.763	-4.266	0.00	0.00	6
ATOM	2925	O	ASP	372	20.893	40.758	-4.709	0.00	0.00	8
ATOM	2926	N	MET	373	19.014	41.907	-4.277	0.00	0.00	7
ATOM	2927	CA	MET	373	18.170	40.910	-4.895	0.00	0.00	6
ATOM	2928	CB	MET	373	17.145	40.386	-3.902	0.00	0.00	6
ATOM	2929	CG	MET	373	17.727	39.704	-2.663	0.00	0.00	6
ATOM	2930	SD	MET	373	16.347	38.918	-1.784	0.00	0.00	16
ATOM	2931	CE	MET	373	15.432	40.310	-1.195	0.00	0.00	6
ATOM	2932	C	MET	373	17.449	41.461	-6.159	0.00	0.00	6
ATOM	2933	O	MET	373	16.714	40.713	-6.808	0.00	0.00	8
ATOM	2934	N	ALA	374	17.604	42.756	-6.486	0.00	0.00	7
ATOM	2935	CA	ALA	374	16.966	43.319	-7.707	0.00	0.00	6
ATOM	2936	CB	ALA	374	16.817	44.826	-7.626	0.00	0.00	6
ATOM	2937	C	ALA	374	17.781	42.911	-8.945	0.00	0.00	6
ATOM	2938	O	ALA	374	17.216	42.464	-9.931	0.00	0.00	8
ATOM	2939	N	CYS	375	19.107	43.021	-8.857	0.00	0.00	7
ATOM	2940	CA	CYS	375	20.036	42.591	-9.923	0.00	0.00	6
ATOM	2941	CB	CYS	375	20.530	43.745	-10.836	0.00	0.00	6
ATOM	2942	SG	CYS	375	19.227	44.512	-11.816	0.00	0.00	16
ATOM	2943	C	CYS	375	21.200	41.889	-9.228	0.00	0.00	6
ATOM	2944	O	CYS	375	22.352	42.340	-9.274	0.00	0.00	8
ATOM	2945	N	ASN	376	20.882	40.754	-8.596	0.00	0.00	7
ATOM	2946	CA	ASN	376	21.859	39.979	-7.842	0.00	0.00	6
ATOM	2947	CB	ASN	376	21.235	38.679	-7.301	0.00	0.00	6
ATOM	2948	CG	ASN	376	21.160	37.559	-8.342	0.00	0.00	6
ATOM	2949	OD1	ASN	376	22.146	36.856	-8.611	0.00	0.00	8
ATOM	2950	ND2	ASN	376	19.981	37.380	-8.909	0.00	0.00	7
ATOM	2951	C	ASN	376	23.172	39.743	-8.579	0.00	0.00	6
ATOM	2952	O	ASN	376	23.210	39.739	-9.808	0.00	0.00	8
ATOM	2953	N	PHE	377	24.257	39.611	-7.815	0.00	0.00	7
ATOM	2954	CA	PHE	377	25.581	39.414	-8.368	0.00	0.00	6
ATOM	2955	CB	PHE	377	26.608	39.345	-7.230	0.00	0.00	6
ATOM	2956	CG	PHE	377	26.650	38.006	-6.544	0.00	0.00	6

Figure 23.23

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ATOM	2957	CD1	PHE	377	27.546	37.009	-6.973	0.00	0.00	6
ATOM	2958	CD2	PHE	377	25.732	37.687	-5.541	0.00	0.00	6
ATOM	2959	CE1	PHE	377	27.505	35.737	-6.409	0.00	0.00	6
ATOM	2960	CE2	PHE	377	25.702	36.407	-4.982	0.00	0.00	6
ATOM	2961	CZ	PHE	377	26.582	35.447	-5.417	0.00	0.00	6
ATOM	2962	C	PHE	377	25.725	38.162	-9.248	0.00	0.00	6
ATOM	2963	O	PHE	377	26.504	38.155	-10.193	0.00	0.00	8
ATOM	2964	N	MET	378	25.019	37.088	-8.909	0.00	0.00	7
ATOM	2965	CA	MET	378	25.152	35.850	-9.667	0.00	0.00	6
ATOM	2966	CB	MET	378	24.545	34.650	-8.905	0.00	0.00	6
ATOM	2967	CG	MET	378	24.953	33.295	-9.501	0.00	0.00	6
ATOM	2968	SD	MET	378	24.600	31.846	-8.493	0.00	0.00	16
ATOM	2969	CE	MET	378	26.143	31.824	-7.695	0.00	0.00	6
ATOM	2970	C	MET	378	24.610	35.957	-11.098	0.00	0.00	6
ATOM	2971	O	MET	378	25.225	35.441	-12.023	0.00	0.00	8
ATOM	2972	N	GLY	379	23.483	36.639	-11.273	0.00	0.00	7
ATOM	2973	CA	GLY	379	22.916	36.827	-12.600	0.00	0.00	6
ATOM	2974	C	GLY	379	23.909	37.491	-13.542	0.00	0.00	6
ATOM	2975	O	GLY	379	24.087	37.054	-14.695	0.00	0.00	8
ATOM	2976	N	ASP	380	24.594	38.516	-13.027	0.00	0.00	7
ATOM	2977	CA	ASP	380	25.599	39.244	-13.790	0.00	0.00	6
ATOM	2978	CB	ASP	380	25.805	40.681	-13.267	0.00	0.00	6
ATOM	2979	CG	ASP	380	24.776	41.666	-13.830	0.00	0.00	6
ATOM	2980	OD1	ASP	380	24.528	41.606	-15.046	0.00	0.00	8
ATOM	2981	OD2	ASP	380	24.210	42.487	-13.059	0.00	0.00	8
ATOM	2982	C	ASP	380	26.920	38.522	-13.897	0.00	0.00	6
ATOM	2983	O	ASP	380	27.678	38.785	-14.828	0.00	0.00	8
ATOM	2984	N	GLU	381	27.240	37.652	-12.942	0.00	0.00	7
ATOM	2985	CA	GLU	381	28.486	36.891	-13.051	0.00	0.00	6
ATOM	2986	CB	GLU	381	28.885	36.216	-11.729	0.00	0.00	6
ATOM	2987	CG	GLU	381	30.186	35.454	-11.899	0.00	0.00	6
ATOM	2988	CD	GLU	381	30.971	35.235	-10.614	0.00	0.00	6
ATOM	2989	OE1	GLU	381	30.421	35.405	-9.499	0.00	0.00	8
ATOM	2990	OE2	GLU	381	32.172	34.904	-10.729	0.00	0.00	8
ATOM	2991	C	GLU	381	28.276	35.846	-14.151	0.00	0.00	6
ATOM	2992	O	GLU	381	29.142	35.598	-14.985	0.00	0.00	8
ATOM	3337	N	THR	423	32.461	41.846	-7.442	0.00	0.00	7
ATOM	3338	CA	THR	423	31.418	41.928	-6.429	0.00	0.00	6
ATOM	3339	CB	THR	423	31.025	40.509	-5.813	0.00	0.00	6
ATOM	3340	OG1	THR	423	32.118	39.973	-5.041	0.00	0.00	8
ATOM	3341	CG2	THR	423	30.632	39.507	-6.916	0.00	0.00	6
ATOM	3342	C	THR	423	31.897	42.867	-5.308	0.00	0.00	6
ATOM	3343	O	THR	423	33.109	43.081	-5.129	0.00	0.00	8
ATOM	3344	N	ILE	424	30.947	43.461	-4.601	0.00	0.00	7
ATOM	3345	CA	ILE	424	31.261	44.318	-3.471	0.00	0.00	6
ATOM	3346	CB	ILE	424	30.743	45.798	-3.651	0.00	0.00	6
ATOM	3347	CG2	ILE	424	30.957	46.572	-2.378	0.00	0.00	6
ATOM	3348	CG1	ILE	424	31.541	46.519	-4.732	0.00	0.00	6
ATOM	3349	CD1	ILE	424	31.051	46.297	-6.131	0.00	0.00	6
ATOM	3350	C	ILE	424	30.564	43.580	-2.297	0.00	0.00	6
ATOM	3351	O	ILE	424	29.328	43.502	-2.233	0.00	0.00	8
ATOM	3352	N	LYS	425	31.369	42.972	-1.429	0.00	0.00	7
ATOM	3353	CA	LYS	425	30.836	42.210	-0.304	0.00	0.00	6
ATOM	3354	CB	LYS	425	31.948	41.450	0.418	0.00	0.00	6
ATOM	3355	CG	LYS	425	31.432	40.315	1.321	0.00	0.00	6
ATOM	3356	CD	LYS	425	32.576	39.443	1.761	0.00	0.00	6
ATOM	3357	CE	LYS	425	33.645	40.231	2.555	0.00	0.00	6
ATOM	3358	NZ	LYS	425	33.124	40.787	3.851	0.00	0.00	7
ATOM	3359	C	LYS	425	30.030	43.030	0.689	0.00	0.00	6

Figure 23.24

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ATOM	3360	O	LYS	425	30.527	43.973	1.265	0.00	0.00	8
ATOM	3361	N	GLY	426	28.802	42.605	0.930	0.00	0.00	7
ATOM	3362	CA	GLY	426	27.949	43.318	1.845	0.00	0.00	6
ATOM	3363	C	GLY	426	27.225	44.514	1.269	0.00	0.00	6
ATOM	3364	O	GLY	426	26.438	45.129	1.979	0.00	0.00	8
ATOM	3365	N	ALA	427	27.488	44.887	0.024	0.00	0.00	7
ATOM	3366	CA	ALA	427	26.777	46.026	-0.547	0.00	0.00	6
ATOM	3367	CB	ALA	427	27.676	46.782	-1.497	0.00	0.00	6
ATOM	3368	C	ALA	427	25.509	45.546	-1.257	0.00	0.00	6
ATOM	3369	O	ALA	427	25.397	44.378	-1.634	0.00	0.00	8
ATOM	3370	N	GLY	428	24.531	46.420	-1.386	0.00	0.00	7
ATOM	3371	CA	GLY	428	23.308	46.065	-2.067	0.00	0.00	6
ATOM	3372	C	GLY	428	23.251	46.665	-3.475	0.00	0.00	6
ATOM	3373	O	GLY	428	24.271	46.940	-4.081	0.00	0.00	8
ATOM	3374	N	HIS	429	22.050	46.931	-3.963	0.00	0.00	7
ATOM	3375	CA	HIS	429	21.827	47.501	-5.287	0.00	0.00	6
ATOM	3376	CB	HIS	429	20.349	47.795	-5.452	0.00	0.00	6
ATOM	3377	CG	HIS	429	19.902	47.920	-6.868	0.00	0.00	6
ATOM	3378	CD2	HIS	429	19.239	48.909	-7.512	0.00	0.00	6
ATOM	3379	ND1	HIS	429	20.044	46.897	-7.779	0.00	0.00	7
ATOM	3380	CE1	HIS	429	19.471	47.241	-8.919	0.00	0.00	6
ATOM	3381	NE2	HIS	429	18.978	48.456	-8.787	0.00	0.00	7
ATOM	3382	C	HIS	429	22.593	48.776	-5.541	0.00	0.00	6
ATOM	3383	O	HIS	429	23.153	48.973	-6.629	0.00	0.00	8
ATOM	3384	N	MET	430	22.569	49.670	-4.559	0.00	0.00	7
ATOM	3385	CA	MET	430	23.236	50.957	-4.665	0.00	0.00	6
ATOM	3386	CB	MET	430	22.297	52.036	-4.162	0.00	0.00	6
ATOM	3387	CG	MET	430	21.019	52.050	-4.968	0.00	0.00	6
ATOM	3388	SD	MET	430	19.807	53.164	-4.342	0.00	0.00	16
ATOM	3389	CE	MET	430	20.554	54.745	-4.772	0.00	0.00	6
ATOM	3390	C	MET	430	24.528	50.927	-3.916	0.00	0.00	6
ATOM	3391	O	MET	430	24.689	51.502	-2.823	0.00	0.00	8
ATOM	3392	N	VAL	431	25.478	50.271	-4.565	0.00	0.00	7
ATOM	3393	CA	VAL	431	26.806	50.048	-4.060	0.00	0.00	6
ATOM	3394	CB	VAL	431	27.684	49.360	-5.167	0.00	0.00	6
ATOM	3395	CG1	VAL	431	29.177	49.533	-4.896	0.00	0.00	6
ATOM	3396	CG2	VAL	431	27.338	47.848	-5.244	0.00	0.00	6
ATOM	3397	C	VAL	431	27.542	51.212	-3.372	0.00	0.00	6
ATOM	3398	O	VAL	431	28.055	51.016	-2.257	0.00	0.00	8
ATOM	3399	N	PRO	432	27.567	52.436	-3.980	0.00	0.00	7
ATOM	3400	CD	PRO	432	27.044	52.899	-5.272	0.00	0.00	6
ATOM	3401	CA	PRO	432	28.279	53.543	-3.332	0.00	0.00	6
ATOM	3402	CB	PRO	432	28.249	54.636	-4.395	0.00	0.00	6
ATOM	3403	CG	PRO	432	28.062	53.906	-5.653	0.00	0.00	6
ATOM	3404	C	PRO	432	27.591	53.999	-2.053	0.00	0.00	6
ATOM	3405	O	PRO	432	28.227	54.508	-1.152	0.00	0.00	8
ATOM	3406	N	THR	433	26.281	53.897	-2.012	0.00	0.00	7
ATOM	3407	CA	THR	433	25.570	54.271	-0.824	0.00	0.00	6
ATOM	3408	CB	THR	433	24.089	54.155	-1.039	0.00	0.00	6
ATOM	3409	OG1	THR	433	23.714	54.976	-2.139	0.00	0.00	8
ATOM	3410	CG2	THR	433	23.341	54.593	0.198	0.00	0.00	6
ATOM	3411	C	THR	433	25.969	53.286	0.288	0.00	0.00	6
ATOM	3412	O	THR	433	26.312	53.701	1.402	0.00	0.00	8
ATOM	3413	N	ASP	434	25.969	51.990	-0.040	0.00	0.00	7
ATOM	3414	CA	ASP	434	26.285	50.953	0.918	0.00	0.00	6
ATOM	3415	CB	ASP	434	25.773	49.612	0.422	0.00	0.00	6
ATOM	3416	CG	ASP	434	24.283	49.562	0.406	0.00	0.00	6
ATOM	3417	OD1	ASP	434	23.640	50.356	1.126	0.00	0.00	8
ATOM	3418	OD2	ASP	434	23.719	48.731	-0.333	0.00	0.00	8
ATOM	3419	C	ASP	434	27.718	50.824	1.402	0.00	0.00	6

Figure 23.25

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ATOM	3420	C	ASP	434	27.937	50.678	2.591	0.00	0.00	8
ATOM	3421	N	LYS	435	28.679	50.871	0.481	0.00	0.00	7
ATOM	3422	CA	LYS	435	30.106	50.746	0.785	0.00	0.00	6
ATOM	3423	CB	LYS	435	30.638	49.403	0.280	0.00	0.00	6
ATOM	3424	CG	LYS	435	29.958	48.181	0.891	0.00	0.00	6
ATOM	3425	CD	LYS	435	30.514	47.886	2.272	0.00	0.00	6
ATOM	3426	CE	LYS	435	29.612	46.931	3.062	0.00	0.00	6
ATOM	3427	NZ	LYS	435	30.222	46.559	4.388	0.00	0.00	7
ATOM	3428	C	LYS	435	30.842	51.851	0.052	0.00	0.00	6
ATOM	3429	O	LYS	435	31.628	51.578	-0.859	0.00	0.00	8
ATOM	3430	N	PRO	436	30.696	53.104	0.510	0.00	0.00	7
ATOM	3431	CD	PRO	436	29.900	53.593	1.652	0.00	0.00	6
ATOM	3432	CA	PRO	436	31.365	54.228	-0.160	0.00	0.00	6
ATOM	3433	CB	PRO	436	31.036	55.423	0.745	0.00	0.00	6
ATOM	3434	CG	PRO	436	30.653	54.806	2.042	0.00	0.00	6
ATOM	3435	C	PRO	436	32.836	54.094	-0.431	0.00	0.00	6
ATOM	3436	O	PRO	436	33.288	54.407	-1.517	0.00	0.00	8

Figure 23.26

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ATOM	3957	N	VAL	1050	15.140	29.530	35.181	1.00	15.73
ATOM	3958	CA	VAL	1050	16.577	29.441	35.363	1.00	14.43
ATOM	3959	CB	VAL	1050	16.982	28.406	36.419	1.00	13.95
ATOM	3960	CG1	VAL	1050	18.474	28.227	36.434	1.00	8.21
ATOM	3961	CG2	VAL	1050	16.510	28.872	37.775	1.00	15.34
ATOM	3962	C	VAL	1050	17.032	29.009	33.986	1.00	14.76
ATOM	3963	O	VAL	1050	16.553	28.007	33.424	1.00	13.00
ATOM	3964	N	VAL	1051	17.897	29.816	33.404	1.00	16.60
ATOM	3965	CA	VAL	1051	18.377	29.535	32.081	1.00	12.64
ATOM	3966	CB	VAL	1051	18.036	30.694	31.142	1.00	10.77
ATOM	3967	CG1	VAL	1051	18.788	30.533	29.820	1.00	16.16
ATOM	3968	CG2	VAL	1051	16.516	30.733	30.920	1.00	6.39
ATOM	3969	C	VAL	1051	19.851	29.284	32.085	1.00	9.28
ATOM	3970	O	VAL	1051	20.626	30.139	32.502	1.00	11.50
ATOM	3971	N	LEU	1052	20.236	28.083	31.679	1.00	11.40
ATOM	3972	CA	LEU	1052	21.648	27.747	31.627	1.00	13.06
ATOM	3973	CB	LEU	1052	21.843	26.230	31.762	1.00	7.02
ATOM	3974	CG	LEU	1052	23.201	25.660	31.327	1.00	11.57
ATOM	3975	CD1	LEU	1052	24.306	26.114	32.254	1.00	9.95
ATOM	3976	CD2	LEU	1052	23.137	24.141	31.274	1.00	10.63
ATOM	3977	C	LEU	1052	22.145	28.195	30.272	1.00	13.38
ATOM	3978	O	LEU	1052	21.449	28.001	29.287	1.00	12.15
ATOM	3979	N	TRP	1053	23.310	28.826	30.218	1.00	12.99
ATOM	3980	CA	TRP	1053	23.874	29.211	28.941	1.00	10.31
ATOM	3981	CB	TRP	1053	24.008	30.728	28.773	1.00	8.17
ATOM	3982	CG	TRP	1053	24.769	31.089	27.475	1.00	4.04
ATOM	3983	CD2	TRP	1053	24.206	31.194	26.154	1.00	2.00
ATOM	3984	CE2	TRP	1053	25.251	31.538	25.278	1.00	2.00
ATOM	3985	CE3	TRP	1053	22.910	31.038	25.633	1.00	2.70
ATOM	3986	CD1	TRP	1053	26.100	31.356	27.342	1.00	2.00
ATOM	3987	NE1	TRP	1053	26.397	31.632	26.026	1.00	5.30
ATOM	3988	CZ2	TRP	1053	25.046	31.736	23.907	1.00	2.00
ATOM	3989	CZ3	TRP	1053	22.709	31.237	24.251	1.00	3.36
ATOM	3990	CH2	TRP	1053	23.775	31.581	23.418	1.00	2.00
ATOM	3991	C	TRP	1053	25.250	28.599	28.795	1.00	7.60
ATOM	3992	O	TRP	1053	26.103	28.778	29.660	1.00	9.96
ATOM	3993	N	LEU	1054	25.463	27.928	27.670	1.00	7.58
ATOM	3994	CA	LEU	1054	26.747	27.323	27.360	1.00	5.66
ATOM	3995	CB	LEU	1054	26.631	25.781	27.347	1.00	9.03
ATOM	3996	CG	LEU	1054	26.265	24.981	28.612	1.00	11.45
ATOM	3997	CD1	LEU	1054	26.086	23.509	28.252	1.00	9.35
ATOM	3998	CD2	LEU	1054	27.350	25.110	29.680	1.00	10.73
ATOM	3999	C	LEU	1054	27.265	27.796	25.993	1.00	7.91
ATOM	4000	O	LEU	1054	26.510	27.853	25.020	1.00	8.23
ATOM	4001	N	ASN	1055	28.527	28.200	25.939	1.00	11.04
ATOM	4002	CA	ASN	1055	29.157	28.594	24.684	1.00	14.62
ATOM	4003	CB	ASN	1055	30.210	29.701	24.876	1.00	10.71
ATOM	4004	CG	ASN	1055	29.596	31.086	24.729	1.00	15.63
ATOM	4005	OD1	ASN	1055	29.153	31.682	25.694	1.00	10.45
ATOM	4006	ND2	ASN	1055	29.479	31.554	23.497	1.00	9.67
ATOM	4007	C	ASN	1055	29.735	27.317	24.101	1.00	16.73
ATOM	4008	O	ASN	1055	29.516	26.247	24.672	1.00	16.00
ATOM	4009	N	GLY	1056	30.450	27.394	22.980	1.00	15.99
ATOM	4010	CA	GLY	1056	30.956	26.167	22.380	1.00	10.17
ATOM	4011	C	GLY	1056	32.431	25.887	22.348	1.00	7.76
ATOM	4012	O	GLY	1056	33.090	25.836	23.370	1.00	10.46
ATOM	4013	N	GLY	1057	32.973	25.745	21.147	1.00	10.50
ATOM	4014	CA	GLY	1057	34.385	25.435	21.003	1.00	7.69
ATOM	4015	C	GLY	1057	34.523	24.142	20.195	1.00	13.35
ATOM	4016	O	GLY	1057	34.239	24.166	18.994	1.00	14.57

Figure 23.27

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ATOM	4017	N	PRO	1058	34.761	22.991	20.838	1.00	12.99
ATOM	4018	CD	PRO	1058	35.011	21.753	20.057	1.00	8.59
ATOM	4019	CA	PRO	1058	34.898	22.727	22.263	1.00	12.12
ATOM	4020	CB	PRO	1058	34.920	21.193	22.318	1.00	10.19
ATOM	4021	CG	PRO	1058	35.678	20.849	21.083	1.00	9.66
ATOM	4022	C	PRO	1058	36.157	23.346	22.876	1.00	11.00
ATOM	4023	O	PRO	1058	37.205	23.415	22.224	1.00	13.72
ATOM	4024	N	GLY	1059	36.019	23.838	24.102	1.00	9.65
ATOM	4025	CA	GLY	1059	37.143	24.460	24.790	1.00	7.94
ATOM	4026	C	GLY	1059	37.040	25.981	24.896	1.00	4.39
ATOM	4027	O	GLY	1059	38.028	26.636	25.214	1.00	5.71
ATOM	4028	N	CYS	1060	35.852	26.539	24.662	1.00	4.99
ATOM	4029	CA	CYS	1060	35.680	27.991	24.724	1.00	9.20
ATOM	4030	C	CYS	1060	34.762	28.409	25.871	1.00	10.91
ATOM	4031	O	CYS	1060	33.866	27.662	26.276	1.00	12.21
ATOM	4032	CB	CYS	1060	35.232	28.568	23.352	1.00	14.45
ATOM	4033	SG	CYS	1060	36.421	28.285	21.964	1.00	12.15
ATOM	4034	N	SER	1061	34.992	29.615	26.385	1.00	15.60
ATOM	4035	CA	SER	1061	34.270	30.119	27.544	1.00	11.61
ATOM	4036	CB	SER	1061	35.145	31.116	28.299	1.00	10.90
ATOM	4037	OG	SER	1061	34.417	31.606	29.408	1.00	17.59
ATOM	4038	C	SER	1061	32.876	30.716	27.414	1.00	10.67
ATOM	4039	O	SER	1061	32.633	31.557	26.560	1.00	16.91
ATOM	4040	N	SER	1062	31.994	30.351	28.348	1.00	8.64
ATOM	4041	CA	SER	1062	30.643	30.886	28.382	1.00	7.49
ATOM	4042	CB	SER	1062	29.753	29.979	29.188	1.00	6.06
ATOM	4043	OG	SER	1062	29.863	28.669	28.670	1.00	8.98
ATOM	4044	C	SER	1062	30.585	32.324	28.924	1.00	5.91
ATOM	4045	O	SER	1062	29.516	32.937	28.979	1.00	9.24
ATOM	4046	N	LEU	1063	31.737	32.851	29.336	1.00	9.64
ATOM	4047	CA	LEU	1063	31.823	34.229	29.826	1.00	9.02
ATOM	4048	CB	LEU	1063	33.047	34.445	30.734	1.00	6.16
ATOM	4049	CG	LEU	1063	33.066	33.666	32.061	1.00	4.88
ATOM	4050	CD1	LEU	1063	34.099	34.285	32.975	1.00	5.60
ATOM	4051	CD2	LEU	1063	31.694	33.633	32.731	1.00	2.93
ATOM	4052	C	LEU	1063	31.897	35.126	28.589	1.00	11.99
ATOM	4053	O	LEU	1063	31.962	36.356	28.694	1.00	13.19
ATOM	4054	N	ASP	1064	31.912	34.477	27.423	1.00	10.79
ATOM	4055	CA	ASP	1064	31.901	35.120	26.114	1.00	7.19
ATOM	4056	CB	ASP	1064	32.324	34.106	25.060	1.00	10.64
ATOM	4057	CG	ASP	1064	32.512	34.703	23.675	1.00	13.89
ATOM	4058	OD1	ASP	1064	32.354	35.921	23.493	1.00	16.35
ATOM	4059	OD2	ASP	1064	32.825	33.939	22.739	1.00	22.07
ATOM	4060	C	ASP	1064	30.437	35.499	25.932	1.00	4.32
ATOM	4061	O	ASP	1064	30.110	36.621	25.581	1.00	11.79
ATOM	4062	N	GLY	1065	29.555	34.556	26.225	1.00	6.64
ATOM	4063	CA	GLY	1065	28.127	34.805	26.140	1.00	5.27
ATOM	4064	C	GLY	1065	27.684	35.909	27.099	1.00	13.37
ATOM	4065	O	GLY	1065	26.712	36.626	26.830	1.00	13.24
ATOM	4066	N	LEU	1066	28.348	36.037	28.244	1.00	14.86
ATOM	4067	CA	LEU	1066	27.987	37.090	29.198	1.00	10.38
ATOM	4068	CB	LEU	1066	28.482	36.762	30.624	1.00	9.13
ATOM	4069	CG	LEU	1066	27.974	37.632	31.800	1.00	5.95
ATOM	4070	CD1	LEU	1066	28.104	36.843	33.076	1.00	9.17
ATOM	4071	CD2	LEU	1066	28.720	38.961	31.951	1.00	5.24
ATOM	4072	C	LEU	1066	28.525	38.451	28.786	1.00	10.31
ATOM	4073	O	LEU	1066	27.758	39.362	28.495	1.00	10.99
ATOM	4074	N	LEU	1067	29.844	38.547	28.722	1.00	9.76
ATOM	4075	CA	LEU	1067	30.532	39.789	28.423	1.00	13.61
ATOM	4076	CB	LEU	1067	32.006	39.671	28.846	1.00	7.85

Figure 23.28

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ATOM	4077	CG	LEU	1067	32.314	39.574	30.347	1.00	8.30
ATOM	4078	CD1	LEU	1067	33.807	39.475	30.541	1.00	6.09
ATOM	4079	CD2	LEU	1067	31.760	40.789	31.082	1.00	5.02
ATOM	4080	C	LEU	1067	30.480	40.351	27.022	1.00	15.33
ATOM	4081	O	LEU	1067	30.828	41.515	26.824	1.00	13.42
ATOM	4082	N	THR	1068	30.153	39.523	26.037	1.00	16.95
ATOM	4083	CA	THR	1068	30.132	40.000	24.651	1.00	12.20
ATOM	4084	CB	THR	1068	31.269	39.397	23.791	1.00	11.32
ATOM	4085	OG1	THR	1068	30.861	38.122	23.290	1.00	22.22
ATOM	4086	CG2	THR	1068	32.544	39.192	24.601	1.00	6.13
ATOM	4087	C	THR	1068	28.832	39.737	23.911	1.00	9.29
ATOM	4088	O	THR	1068	28.621	40.312	22.853	1.00	8.35
ATOM	4089	N	GLU	1069	27.964	38.879	24.455	1.00	9.66
ATOM	4090	CA	GLU	1069	26.713	38.579	23.779	1.00	2.87
ATOM	4091	CB	GLU	1069	26.603	37.092	23.474	1.00	2.00
ATOM	4092	CG	GLU	1069	27.747	36.517	22.732	1.00	2.00
ATOM	4093	CD	GLU	1069	27.440	35.072	22.388	1.00	10.44
ATOM	4094	OE1	GLU	1069	28.014	34.140	22.979	1.00	13.18
ATOM	4095	OE2	GLU	1069	26.540	34.866	21.568	1.00	7.99
ATOM	4096	C	GLU	1069	25.432	39.016	24.453	1.00	8.48
ATOM	4097	O	GLU	1069	24.713	39.883	23.946	1.00	12.89
ATOM	4098	N	HIS	1070	25.075	38.356	25.548	1.00	7.61
ATOM	4099	CA	HIS	1070	23.827	38.713	26.204	1.00	7.18
ATOM	4100	CB	HIS	1070	22.664	37.820	25.691	1.00	12.98
ATOM	4101	CG	HIS	1070	22.907	36.344	25.802	1.00	15.52
ATOM	4102	CD2	HIS	1070	22.567	35.319	24.987	1.00	12.57
ATOM	4103	ND1	HIS	1070	23.563	35.767	26.874	1.00	20.02
ATOM	4104	CE1	HIS	1070	23.609	34.458	26.711	1.00	10.15
ATOM	4105	NE2	HIS	1070	23.014	34.164	25.574	1.00	14.92
ATOM	4106	C	HIS	1070	23.816	38.902	27.733	1.00	9.42
ATOM	4107	O	HIS	1070	22.759	38.806	28.379	1.00	11.06
ATOM	4108	N	GLY	1071	24.988	39.196	28.291	1.00	12.09
ATOM	4109	CA	GLY	1071	25.060	39.442	29.711	1.00	15.45
ATOM	4110	C	GLY	1071	24.440	40.792	30.089	1.00	17.58
ATOM	4111	O	GLY	1071	24.138	41.618	29.200	1.00	11.30
ATOM	4112	N	PRO	1072	24.226	41.043	31.406	1.00	16.14
ATOM	4113	CD	PRO	1072	24.537	40.154	32.538	1.00	11.01
ATOM	4114	CA	PRO	1072	23.629	42.305	31.886	1.00	14.40
ATOM	4115	CB	PRO	1072	23.425	42.029	33.379	1.00	11.56
ATOM	4116	CG	PRO	1072	24.565	41.112	33.699	1.00	13.32
ATOM	4117	C	PRO	1072	24.484	43.541	31.600	1.00	11.41
ATOM	4118	O	PRO	1072	23.985	44.675	31.625	1.00	14.15
ATOM	4119	N	PHE	1073	25.757	43.308	31.304	1.00	10.67
ATOM	4120	CA	PHE	1073	26.719	44.350	30.958	1.00	11.47
ATOM	4121	CB	PHE	1073	27.452	44.906	32.194	1.00	14.42
ATOM	4122	CG	PHE	1073	27.569	43.926	33.341	1.00	12.17
ATOM	4123	CD1	PHE	1073	26.753	44.067	34.460	1.00	11.62
ATOM	4124	CD2	PHE	1073	28.462	42.849	33.280	1.00	12.34
ATOM	4125	CE1	PHE	1073	26.815	43.152	35.501	1.00	9.61
ATOM	4126	CE2	PHE	1073	28.536	41.926	34.312	1.00	14.52
ATOM	4127	CZ	PHE	1073	27.704	42.076	35.432	1.00	11.76
ATOM	4128	C	PHE	1073	27.710	43.707	29.994	1.00	11.39
ATOM	4129	O	PHE	1073	27.894	42.494	30.008	1.00	11.75
ATOM	4130	N	LEU	1074	28.369	44.521	29.182	1.00	13.78
ATOM	4131	CA	LEU	1074	29.302	44.007	28.198	1.00	13.58
ATOM	4132	CB	LEU	1074	28.725	44.228	26.794	1.00	10.75
ATOM	4133	CG	LEU	1074	27.320	43.656	26.597	1.00	9.26
ATOM	4134	CD1	LEU	1074	26.733	44.121	25.289	1.00	13.37
ATOM	4135	CD2	LEU	1074	27.371	42.133	26.651	1.00	7.69
ATOM	4136	C	LEU	1074	30.594	44.742	28.330	1.00	13.92

Figure 23.29

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ATOM	4137	O	LEU	1074	30.588	45.934	28.585	1.00	15.49
ATOM	4138	N	VAL	1075	31.704	44.036	28.182	1.00	12.83
ATOM	4139	CA	VAL	1075	33.007	44.651	28.290	1.00	15.13
ATOM	4140	CB	VAL	1075	34.157	43.587	28.414	1.00	16.03
ATOM	4141	CG1	VAL	1075	34.194	42.650	27.197	1.00	15.81
ATOM	4142	CG2	VAL	1075	35.499	44.270	28.604	1.00	12.30
ATOM	4143	C	VAL	1075	33.206	45.579	27.098	1.00	17.47
ATOM	4144	O	VAL	1075	32.715	45.328	25.987	1.00	17.39
ATOM	4145	N	GLN	1076	33.928	46.663	27.340	1.00	17.37
ATOM	4146	CA	GLN	1076	34.189	47.660	26.327	1.00	14.53
ATOM	4147	CB	GLN	1076	34.018	49.062	26.944	1.00	19.73
ATOM	4148	CG	GLN	1076	32.615	49.311	27.499	1.00	16.49
ATOM	4149	CD	GLN	1076	31.532	49.111	26.450	1.00	20.70
ATOM	4150	OE1	GLN	1076	31.431	49.886	25.510	1.00	27.97
ATOM	4151	NE2	GLN	1076	30.719	48.086	26.614	1.00	20.69
ATOM	4152	C	GLN	1076	35.568	47.472	25.755	1.00	13.22
ATOM	4153	O	GLN	1076	36.375	46.721	26.301	1.00	14.01
ATOM	4697	N	LEU	1144	13.206	25.412	34.159	1.00	13.22
ATOM	4698	CA	LEU	1144	14.571	25.382	33.699	1.00	13.56
ATOM	4699	CB	LEU	1144	15.264	24.198	34.367	1.00	10.34
ATOM	4700	CG	LEU	1144	16.655	23.779	33.916	1.00	8.49
ATOM	4701	CD1	LEU	1144	17.704	24.805	34.343	1.00	5.67
ATOM	4702	CD2	LEU	1144	16.958	22.392	34.498	1.00	10.36
ATOM	4703	C	LEU	1144	14.628	25.232	32.175	1.00	16.10
ATOM	4704	O	LEU	1144	13.863	24.469	31.588	1.00	18.50
ATOM	4705	N	PHE	1145	15.544	25.957	31.542	1.00	16.40
ATOM	4706	CA	PHE	1145	15.722	25.895	30.098	1.00	13.20
ATOM	4707	CB	PHE	1145	15.246	27.192	29.436	1.00	14.23
ATOM	4708	CG	PHE	1145	13.755	27.350	29.421	1.00	16.54
ATOM	4709	CD1	PHE	1145	13.090	27.958	30.485	1.00	17.20
ATOM	4710	CD2	PHE	1145	13.008	26.900	28.343	1.00	16.49
ATOM	4711	CE1	PHE	1145	11.698	28.112	30.471	1.00	15.56
ATOM	4712	CE2	PHE	1145	11.612	27.053	28.318	1.00	14.48
ATOM	4713	CZ	PHE	1145	10.958	27.658	29.383	1.00	16.77
ATOM	4714	C	PHE	1145	17.208	25.733	29.892	1.00	14.21
ATOM	4715	O	PHE	1145	17.990	26.336	30.638	1.00	15.28
ATOM	4716	N	LEU	1146	17.606	24.859	28.972	1.00	13.91
ATOM	4717	CA	LEU	1146	19.032	24.646	28.685	1.00	10.47
ATOM	4718	CB	LEU	1146	19.352	23.134	28.658	1.00	9.43
ATOM	4719	CG	LEU	1146	18.791	22.331	29.855	1.00	9.20
ATOM	4720	CD1	LEU	1146	18.952	20.829	29.653	1.00	8.44
ATOM	4721	CD2	LEU	1146	19.519	22.741	31.125	1.00	5.27
ATOM	4722	C	LEU	1146	19.318	25.338	27.324	1.00	10.63
ATOM	4723	O	LEU	1146	18.695	25.011	26.318	1.00	10.44
ATOM	4724	N	THR	1147	20.214	26.325	27.315	1.00	14.19
ATOM	4725	CA	THR	1147	20.537	27.090	26.113	1.00	9.23
ATOM	4726	CB	THR	1147	19.914	28.551	26.148	1.00	5.47
ATOM	4727	OG1	THR	1147	20.546	29.352	27.154	1.00	10.68
ATOM	4728	CG2	THR	1147	18.449	28.512	26.411	1.00	2.00
ATOM	4729	C	THR	1147	22.038	27.176	25.859	1.00	8.62
ATOM	4730	O	THR	1147	22.843	27.037	26.781	1.00	9.01
ATOM	4731	N	GLY	1148	22.419	27.406	24.603	1.00	7.75
ATOM	4732	CA	GLY	1148	23.829	27.484	24.272	1.00	3.58
ATOM	4733	C	GLY	1148	24.059	27.842	22.824	1.00	4.46
ATOM	4734	O	GLY	1148	23.128	28.015	22.049	1.00	3.11
ATOM	4735	N	GLU	1149	25.304	27.808	22.413	1.00	7.23
ATOM	4736	CA	GLU	1149	25.627	28.188	21.066	1.00	9.10
ATOM	4737	CB	GLU	1149	26.010	29.673	21.109	1.00	7.91
ATOM	4738	CG	GLU	1149	26.471	30.328	19.819	1.00	4.32

Figure 23.30

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ATOM	4739	CD	GLU	1149	27.043	31.704	20.104	1.00	3.75
ATOM	4740	OE1	GLU	1149	28.288	31.863	20.114	1.00	5.72
ATOM	4741	OE2	GLU	1149	26.236	32.626	20.338	1.00	8.13
ATOM	4742	C	GLU	1149	26.788	27.406	20.486	1.00	7.02
ATOM	4743	O	GLU	1149	27.669	26.958	21.220	1.00	11.07
ATOM	4744	N	SER	1150	26.762	27.246	19.160	1.00	7.15
ATOM	4745	CA	SER	1150	27.841	26.611	18.408	1.00	4.85
ATOM	4746	CB	SER	1150	29.103	27.442	18.628	1.00	3.37
ATOM	4747	OG	SER	1150	30.153	27.159	17.725	1.00	14.60
ATOM	4748	C	SER	1150	28.032	25.143	18.779	1.00	6.96
ATOM	4749	O	SER	1150	27.137	24.326	18.535	1.00	6.55
ATOM	4750	N	TYR	1151	29.148	24.798	19.415	1.00	7.04
ATOM	4751	CA	TYR	1151	29.366	23.400	19.796	1.00	7.55
ATOM	4752	CB	TYR	1151	30.781	23.140	20.272	1.00	9.49
ATOM	4753	CG	TYR	1151	31.118	21.671	20.242	1.00	15.57
ATOM	4754	CD1	TYR	1151	31.584	21.073	19.075	1.00	14.31
ATOM	4755	CE1	TYR	1151	31.839	19.721	19.021	1.00	13.43
ATOM	4756	CD2	TYR	1151	30.924	20.864	21.362	1.00	15.31
ATOM	4757	CE2	TYR	1151	31.172	19.509	21.315	1.00	11.83
ATOM	4758	CZ	TYR	1151	31.623	18.943	20.142	1.00	13.92
ATOM	4759	OH	TYR	1151	31.811	17.595	20.059	1.00	9.48
ATOM	4760	C	TYR	1151	28.369	22.966	20.853	1.00	6.75
ATOM	4761	O	TYR	1151	28.084	21.778	20.974	1.00	13.35
ATOM	4762	N	ALA	1152	27.788	23.929	21.577	1.00	5.99
ATOM	4763	CA	ALA	1152	26.767	23.616	22.559	1.00	2.00
ATOM	4764	CB	ALA	1152	26.383	24.820	23.321	1.00	4.52
ATOM	4765	C	ALA	1152	25.553	23.032	21.857	1.00	4.59
ATOM	4766	O	ALA	1152	24.548	22.702	22.493	1.00	5.46
ATOM	4767	N	GLY	1153	25.605	22.953	20.530	1.00	7.41
ATOM	4768	CA	GLY	1153	24.507	22.360	19.800	1.00	2.72
ATOM	4769	C	GLY	1153	24.631	20.862	20.044	1.00	5.28
ATOM	4770	O	GLY	1153	23.700	20.112	19.769	1.00	8.08
ATOM	4771	N	ILE	1154	25.833	20.442	20.443	1.00	8.44
ATOM	4772	CA	ILE	1154	26.130	19.057	20.827	1.00	8.33
ATOM	4773	CB	ILE	1154	27.600	18.690	20.531	1.00	8.67
ATOM	4774	CG2	ILE	1154	27.908	17.283	21.043	1.00	2.60
ATOM	4775	CG1	ILE	1154	27.941	18.880	19.037	1.00	8.20
ATOM	4776	CD1	ILE	1154	27.561	17.739	18.132	1.00	9.74
ATOM	4777	C	ILE	1154	25.914	18.990	22.363	1.00	10.50
ATOM	4778	O	ILE	1154	25.100	18.194	22.844	1.00	12.69
ATOM	4779	N	TYR	1155	26.624	19.857	23.107	1.00	12.77
ATOM	4780	CA	TYR	1155	26.518	19.961	24.578	1.00	11.74
ATOM	4781	CB	TYR	1155	27.161	21.253	25.132	1.00	3.22
ATOM	4782	CG	TYR	1155	28.662	21.395	25.000	1.00	2.00
ATOM	4783	CD1	TYR	1155	29.253	22.658	24.927	1.00	2.74
ATOM	4784	CE1	TYR	1155	30.635	22.802	24.824	1.00	2.40
ATOM	4785	CD2	TYR	1155	29.486	20.285	24.964	1.00	4.07
ATOM	4786	CE2	TYR	1155	30.869	20.416	24.855	1.00	3.82
ATOM	4787	CZ	TYR	1155	31.439	21.670	24.793	1.00	2.00
ATOM	4788	OH	TYR	1155	32.819	21.785	24.754	1.00	3.24
ATOM	4789	C	TYR	1155	25.075	19.965	25.066	1.00	12.15
ATOM	4790	O	TYR	1155	24.698	19.119	25.870	1.00	18.34
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ATOM	4919	N	GLY	1173	12.464	23.418	28.523	1.00	12.94
ATOM	4920	CA	GLY	1173	12.808	23.564	27.126	1.00	12.85
ATOM	4921	C	GLY	1173	14.259	23.786	26.878	1.00	10.63
ATOM	4922	O	GLY	1173	15.052	23.822	27.820	1.00	15.71
ATOM	4923	N	LEU	1174	14.605	23.920	25.606	1.00	15.11
ATOM	4924	CA	LEU	1174	15.986	24.147	25.181	1.00	17.83
ATOM	4925	CB	LEU	1174	16.753	22.808	25.033	1.00	18.83

Figure 23.31

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ATOM	4926	CG	LEU	1174	16.324	21.627	24.139	1.00	21.15
ATOM	4927	CD1	LEU	1174	17.570	20.903	23.670	1.00	18.66
ATOM	4928	CD2	LEU	1174	15.384	20.660	24.875	1.00	16.90
ATOM	4929	C	LEU	1174	16.066	24.978	23.891	1.00	16.86
ATOM	4930	O	LEU	1174	15.197	24.872	23.032	1.00	16.96
ATOM	4931	N	ALA	1175	17.117	25.785	23.757	1.00	16.09
ATOM	4932	CA	ALA	1175	17.315	26.636	22.584	1.00	13.66
ATOM	4933	CB	ALA	1175	16.831	28.064	22.877	1.00	10.96
ATOM	4934	C	ALA	1175	18.808	26.626	22.238	1.00	11.09
ATOM	4935	O	ALA	1175	19.646	26.733	23.128	1.00	9.89
ATOM	4936	N	VAL	1176	19.136	26.429	20.961	1.00	8.95
ATOM	4937	CA	VAL	1176	20.527	26.368	20.507	1.00	9.56
ATOM	4938	CB	VAL	1176	20.881	24.923	20.037	1.00	11.73
ATOM	4939	CG1	VAL	1176	22.204	24.905	19.271	1.00	5.65
ATOM	4940	CG2	VAL	1176	20.971	23.991	21.227	1.00	8.28
ATOM	4941	C	VAL	1176	20.754	27.340	19.342	1.00	11.14
ATOM	4942	O	VAL	1176	20.033	27.277	18.350	1.00	11.32
ATOM	4943	N	GLY	1177	21.747	28.222	19.454	1.00	14.54
ATOM	4944	CA	GLY	1177	22.020	29.172	18.384	1.00	10.12
ATOM	4945	C	GLY	1177	23.123	28.723	17.463	1.00	8.78
ATOM	4946	O	GLY	1177	24.217	28.404	17.930	1.00	4.07
ATOM	4947	N	ASN	1178	22.871	28.722	16.162	1.00	8.51
ATOM	4948	CA	ASN	1178	23.891	28.266	15.205	1.00	5.20
ATOM	4949	CB	ASN	1178	24.882	29.381	14.874	1.00	6.09
ATOM	4950	CG	ASN	1178	24.253	30.496	14.080	1.00	10.75
ATOM	4951	OD1	ASN	1178	23.518	31.319	14.632	1.00	9.79
ATOM	4952	ND2	ASN	1178	24.485	30.503	12.766	1.00	10.54
ATOM	4953	C	ASN	1178	24.642	27.062	15.770	1.00	2.90
ATOM	4954	O	ASN	1178	25.867	27.062	15.864	1.00	4.70
ATOM	4955	N	GLY	1179	23.895	26.031	16.128	1.00	7.96
ATOM	4956	CA	GLY	1179	24.520	24.867	16.717	1.00	13.63
ATOM	4957	C	GLY	1179	24.984	23.838	15.723	1.00	14.42
ATOM	4958	O	GLY	1179	24.437	23.747	14.630	1.00	17.43
ATOM	4959	N	LEU	1180	25.982	23.056	16.129	1.00	11.44
ATOM	4960	CA	LEU	1180	26.549	21.979	15.324	1.00	7.41
ATOM	4961	CB	LEU	1180	27.971	21.716	15.766	1.00	8.30
ATOM	4962	CG	LEU	1180	28.874	20.795	14.975	1.00	12.32
ATOM	4963	CD1	LEU	1180	29.132	21.344	13.594	1.00	11.76
ATOM	4964	CD2	LEU	1180	30.162	20.722	15.743	1.00	7.94
ATOM	4965	C	LEU	1180	25.726	20.736	15.588	1.00	10.39
ATOM	4966	O	LEU	1180	26.137	19.888	16.357	1.00	20.58
ATOM	4967	N	SER	1181	24.562	20.641	14.954	1.00	7.38
ATOM	4968	CA	SER	1181	23.665	19.505	15.117	1.00	5.37
ATOM	4969	CB	SER	1181	22.252	19.919	14.728	1.00	3.06
ATOM	4970	OG	SER	1181	21.898	21.130	15.352	1.00	8.63
ATOM	4971	C	SER	1181	24.088	18.253	14.336	1.00	7.63
ATOM	4972	O	SER	1181	23.870	17.149	14.773	1.00	9.69
ATOM	4973	N	SER	1182	24.681	18.446	13.171	1.00	13.08
ATOM	4974	CA	SER	1182	25.129	17.359	12.326	1.00	9.50
ATOM	4975	CB	SER	1182	23.999	16.922	11.392	1.00	11.96
ATOM	4976	OG	SER	1182	24.484	16.052	10.380	1.00	13.63
ATOM	4977	C	SER	1182	26.284	17.862	11.496	1.00	11.32
ATOM	4978	O	SER	1182	26.147	18.831	10.753	1.00	11.11
ATOM	4979	N	TYR	1183	27.433	17.216	11.639	1.00	8.38
ATOM	4980	CA	TYR	1183	28.638	17.577	10.892	1.00	7.66
ATOM	4981	CB	TYR	1183	29.815	16.711	11.324	1.00	6.76
ATOM	4982	CG	TYR	1183	30.179	16.800	12.795	1.00	10.68
ATOM	4983	CD1	TYR	1183	29.492	16.044	13.753	1.00	10.39
ATOM	4984	CE1	TYR	1183	29.837	16.105	15.104	1.00	13.19
ATOM	4985	CD2	TYR	1183	31.216	17.617	13.223	1.00	3.47

Figure 23.32

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ATOM	4986	CE2	TYR	1183	31.568	17.688	14.582	1.00	8.20
ATOM	4987	CZ	TYR	1183	30.875	16.929	15.515	1.00	4.50
ATOM	4988	OH	TYR	1183	31.224	17.007	16.840	1.00	8.71
ATOM	4989	C	TYR	1183	28.427	17.396	9.394	1.00	11.19
ATOM	4990	O	TYR	1183	28.933	18.157	8.604	1.00	16.20
ATOM	4991	N	GLU	1184	27.681	16.374	9.006	1.00	11.16
ATOM	4992	CA	GLU	1184	27.427	16.102	7.595	1.00	9.88
ATOM	4993	CB	GLU	1184	26.762	14.734	7.455	1.00	13.18
ATOM	4994	CG	GLU	1184	26.589	14.271	6.029	1.00	22.28
ATOM	4995	CD	GLU	1184	26.046	12.858	5.926	1.00	23.99
ATOM	4996	OE1	GLU	1184	25.844	12.212	6.979	1.00	29.76
ATOM	4997	OE2	GLU	1184	25.836	12.386	4.784	1.00	25.06
ATOM	4998	C	GLU	1184	26.557	17.162	6.942	1.00	5.08
ATOM	4999	O	GLU	1184	26.876	17.654	5.869	1.00	7.62
ATOM	5000	N	GLN	1185	25.422	17.456	7.560	1.00	4.87
ATOM	5001	CA	GLN	1185	24.505	18.459	7.046	1.00	7.10
ATOM	5002	CB	GLN	1185	23.190	18.424	7.810	1.00	8.55
ATOM	5003	CG	GLN	1185	22.230	17.406	7.217	1.00	11.60
ATOM	5004	CD	GLN	1185	21.068	17.092	8.123	1.00	16.98
ATOM	5005	OE1	GLN	1185	20.012	16.646	7.667	1.00	26.08
ATOM	5006	NE2	GLN	1185	21.253	17.306	9.424	1.00	25.40
ATOM	5007	C	GLN	1185	25.123	19.846	7.073	1.00	11.26
ATOM	5008	O	GLN	1185	24.827	20.671	6.213	1.00	15.21
ATOM	5009	N	ASN	1186	26.029	20.070	8.019	1.00	12.87
ATOM	5010	CA	ASN	1186	26.731	21.337	8.153	1.00	8.85
ATOM	5011	CB	ASN	1186	27.362	21.458	9.548	1.00	4.66
ATOM	5012	CG	ASN	1186	28.040	22.814	9.773	1.00	3.46
ATOM	5013	OD1	ASN	1186	29.189	22.896	10.220	1.00	12.07
ATOM	5014	ND2	ASN	1186	27.325	23.881	9.447	1.00	4.40
ATOM	5015	C	ASN	1186	27.811	21.479	7.069	1.00	7.58
ATOM	5016	O	ASN	1186	27.874	22.492	6.385	1.00	12.11
ATOM	5017	N	ASP	1187	28.652	20.463	6.906	1.00	6.80
ATOM	5018	CA	ASP	1187	29.722	20.500	5.907	1.00	6.70
ATOM	5019	CB	ASP	1187	30.589	19.253	5.985	1.00	10.91
ATOM	5020	CG	ASP	1187	31.414	19.182	7.256	1.00	14.86
ATOM	5021	OD1	ASP	1187	31.598	20.223	7.929	1.00	14.90
ATOM	5022	OD2	ASP	1187	31.892	18.062	7.570	1.00	16.93
ATOM	5023	C	ASP	1187	29.178	20.612	4.490	1.00	11.55
ATOM	5024	O	ASP	1187	29.749	21.331	3.675	1.00	13.94
ATOM	5025	N	ASN	1188	28.123	19.851	4.187	1.00	8.53
ATOM	5026	CA	ASN	1188	27.484	19.876	2.863	1.00	9.33
ATOM	5027	CB	ASN	1188	26.418	18.784	2.725	1.00	4.69
ATOM	5028	CG	ASN	1188	27.000	17.387	2.563	1.00	6.21
ATOM	5029	OD1	ASN	1188	28.105	17.195	2.045	1.00	11.05
ATOM	5030	ND2	ASN	1188	26.232	16.397	2.989	1.00	9.02
ATOM	5031	C	ASN	1188	26.805	21.222	2.549	1.00	9.45
ATOM	5032	O	ASN	1188	27.022	21.777	1.482	1.00	12.60
ATOM	5033	N	SER	1189	25.922	21.694	3.434	1.00	12.40
ATOM	5034	CA	SER	1189	25.213	22.976	3.234	1.00	8.14
ATOM	5035	CB	SER	1189	24.209	23.248	4.369	1.00	11.33
ATOM	5036	OG	SER	1189	24.838	23.336	5.639	1.00	14.66
ATOM	5037	C	SER	1189	26.163	24.172	3.066	1.00	5.20
ATOM	5038	O	SER	1189	25.848	25.107	2.341	1.00	10.13
ATOM	5039	N	LEU	1190	27.321	24.108	3.726	1.00	4.88
ATOM	5040	CA	LEU	1190	28.347	25.144	3.676	1.00	7.24
ATOM	5041	CB	LEU	1190	29.492	24.841	4.660	1.00	5.16
ATOM	5042	CG	LEU	1190	30.769	25.694	4.538	1.00	4.08
ATOM	5043	CD1	LEU	1190	30.472	27.146	4.898	1.00	8.34
ATOM	5044	CD2	LEU	1190	31.844	25.167	5.418	1.00	5.42
ATOM	5045	C	LEU	1190	28.958	25.322	2.304	1.00	12.23

Figure 23.33

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ATOM	5046	O	LEU	1190	29.261	26.448	1.910	1.00	14.63
ATOM	5047	N	VAL	1191	29.240	24.209	1.617	1.00	11.86
ATOM	5048	CA	VAL	1191	29.818	24.294	0.283	1.00	7.71
ATOM	5049	CB	VAL	1191	30.236	22.927	-0.261	1.00	10.40
ATOM	5050	CG1	VAL	1191	30.927	23.113	-1.605	1.00	5.34
ATOM	5051	CG2	VAL	1191	31.255	22.298	0.683	1.00	2.48
ATOM	5052	C	VAL	1191	28.826	25.015	-0.621	1.00	6.93
ATOM	5053	O	VAL	1191	29.202	25.900	-1.367	1.00	9.05
ATOM	5054	N	TYR	1192	27.555	24.669	-0.503	1.00	7.63
ATOM	5055	CA	TYR	1192	26.493	25.330	-1.249	1.00	11.42
ATOM	5056	CB	TYR	1192	25.172	24.681	-0.884	1.00	14.20
ATOM	5057	CG	TYR	1192	24.927	23.392	-1.587	1.00	19.34
ATOM	5058	CD1	TYR	1192	25.410	22.187	-1.091	1.00	18.62
ATOM	5059	CE1	TYR	1192	25.175	21.003	-1.763	1.00	19.90
ATOM	5060	CD2	TYR	1192	24.206	23.377	-2.763	1.00	20.70
ATOM	5061	CE2	TYR	1192	23.964	22.209	-3.440	1.00	16.84
ATOM	5062	CZ	TYR	1192	24.441	21.028	-2.946	1.00	18.91
ATOM	5063	OH	TYR	1192	24.141	19.892	-3.653	1.00	19.39
ATOM	5064	C	TYR	1192	26.413	26.827	-0.851	1.00	15.42
ATOM	5065	O	TYR	1192	26.256	27.713	-1.696	1.00	13.38
ATOM	5066	N	PHE	1193	26.395	27.076	0.455	1.00	12.57
ATOM	5067	CA	PHE	1193	26.346	28.419	1.014	1.00	10.64
ATOM	5068	CB	PHE	1193	26.592	28.348	2.545	1.00	7.63
ATOM	5069	CG	PHE	1193	26.377	29.653	3.262	1.00	5.57
ATOM	5070	CD1	PHE	1193	25.185	29.901	3.928	1.00	3.60
ATOM	5071	CD2	PHE	1193	27.350	30.652	3.233	1.00	3.09
ATOM	5072	CE1	PHE	1193	24.960	31.138	4.559	1.00	5.95
ATOM	5073	CE2	PHE	1193	27.134	31.885	3.851	1.00	2.00
ATOM	5074	CZ	PHE	1193	25.941	32.125	4.513	1.00	2.00
ATOM	5075	C	PHE	1193	27.419	29.267	0.337	1.00	4.40
ATOM	5076	O	PHE	1193	27.135	30.351	-0.159	1.00	7.94
ATOM	5077	N	ALA	1194	28.640	28.749	0.298	1.00	2.95
ATOM	5078	CA	ALA	1194	29.783	29.440	-0.292	1.00	5.66
ATOM	5079	CB	ALA	1194	31.050	28.646	-0.098	1.00	4.86
ATOM	5080	C	ALA	1194	29.624	29.831	-1.765	1.00	10.74
ATOM	5081	O	ALA	1194	30.001	30.935	-2.147	1.00	12.73
ATOM	5082	N	TYR	1195	29.114	28.936	-2.609	1.00	12.02
ATOM	5083	CA	TYR	1195	28.940	29.297	-4.007	1.00	9.05
ATOM	5084	CB	TYR	1195	28.530	28.086	-4.850	1.00	12.04
ATOM	5085	CG	TYR	1195	28.251	28.445	-6.310	1.00	7.57
ATOM	5086	CD1	TYR	1195	29.250	29.024	-7.113	1.00	2.00
ATOM	5087	CE1	TYR	1195	29.007	29.342	-8.466	1.00	3.93
ATOM	5088	CD2	TYR	1195	26.996	28.188	-6.887	1.00	4.93
ATOM	5089	CE2	TYR	1195	26.739	28.488	-8.242	1.00	12.14
ATOM	5090	CZ	TYR	1195	27.756	29.064	-9.026	1.00	5.79
ATOM	5091	OH	TYR	1195	27.526	29.304	-10.363	1.00	7.94
ATOM	5092	C	TYR	1195	27.889	30.384	-4.175	1.00	7.65
ATOM	5093	O	TYR	1195	28.108	31.366	-4.870	1.00	13.56
ATOM	5094	N	TYR	1196	26.742	30.194	-3.541	1.00	4.57
ATOM	5095	CA	TYR	1196	25.638	31.115	-3.652	1.00	5.37
ATOM	5096	CB	TYR	1196	24.358	30.406	-3.290	1.00	5.49
ATOM	5097	CG	TYR	1196	24.031	29.328	-4.306	1.00	12.37
ATOM	5098	CD1	TYR	1196	24.480	28.014	-4.134	1.00	7.05
ATOM	5099	CE1	TYR	1196	24.208	27.030	-5.068	1.00	9.49
ATOM	5100	CD2	TYR	1196	23.296	29.626	-5.451	1.00	12.25
ATOM	5101	CE2	TYR	1196	23.014	28.657	-6.392	1.00	13.86
ATOM	5102	CZ	TYR	1196	23.473	27.356	-6.199	1.00	15.48
ATOM	5103	OH	TYR	1196	23.192	26.397	-7.144	1.00	17.66
ATOM	5104	C	TYR	1196	25.778	32.445	-2.949	1.00	8.50
ATOM	5105	O	TYR	1196	24.955	33.333	-3.137	1.00	10.82

Figure 23.34

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ATOM	5106	N	HIS	1197	26.815	32.567	-2.127	1.00	9.62
ATOM	5107	CA	HIS	1197	27.114	33.807	-1.414	1.00	6.06
ATOM	5108	CB	HIS	1197	27.325	33.566	0.079	1.00	2.90
ATOM	5109	CG	HIS	1197	26.050	33.370	0.825	1.00	2.00
ATOM	5110	CD2	HIS	1197	25.331	34.214	1.598	1.00	2.00
ATOM	5111	ND1	HIS	1197	25.295	32.224	0.717	1.00	2.00
ATOM	5112	CE1	HIS	1197	24.160	32.371	1.376	1.00	2.00
ATOM	5113	NE2	HIS	1197	24.162	33.573	1.923	1.00	2.00
ATOM	5114	C	HIS	1197	28.336	34.424	-2.085	1.00	8.83
ATOM	5115	O	HIS	1197	28.984	35.305	-1.538	1.00	15.06
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ATOM	5341	N	LEU	1226	39.631	11.780	-5.534	1.00	15.25
ATOM	5342	CA	LEU	1226	40.781	12.643	-5.687	1.00	23.06
ATOM	5343	CB	LEU	1226	41.769	11.961	-6.604	1.00	26.67
ATOM	5344	CG	LEU	1226	43.087	11.890	-5.864	1.00	35.66
ATOM	5345	CD1	LEU	1226	43.737	10.548	-6.101	1.00	38.32
ATOM	5346	CD2	LEU	1226	43.966	13.069	-6.308	1.00	35.54
ATOM	5347	C	LEU	1226	40.616	14.131	-6.071	1.00	25.04
ATOM	5348	O	LEU	1226	41.053	15.016	-5.338	1.00	27.76
ATOM	5349	N	GLU	1227	40.022	14.426	-7.221	1.00	25.04
ATOM	5350	CA	GLU	1227	39.878	15.831	-7.600	1.00	24.73
ATOM	5351	CB	GLU	1227	39.645	16.003	-9.110	1.00	32.37
ATOM	5352	CG	GLU	1227	40.211	17.335	-9.681	1.00	45.99
ATOM	5353	CD	GLU	1227	41.761	17.469	-9.612	1.00	57.33
ATOM	5354	OE1	GLU	1227	42.430	16.824	-8.757	1.00	58.99
ATOM	5355	OE2	GLU	1227	42.320	18.250	-10.424	1.00	62.92
ATOM	5356	C	GLU	1227	38.798	16.542	-6.796	1.00	20.14
ATOM	5357	O	GLU	1227	38.804	17.765	-6.682	1.00	17.51
ATOM	5358	N	CYS	1228	37.855	15.774	-6.269	1.00	16.01
ATOM	5359	CA	CYS	1228	36.805	16.341	-5.452	1.00	20.09
ATOM	5360	C	CYS	1228	37.436	16.918	-4.194	1.00	20.43
ATOM	5361	O	CYS	1228	37.133	18.038	-3.797	1.00	20.36
ATOM	5362	CB	CYS	1228	35.819	15.276	-5.032	1.00	17.24
ATOM	5363	SG	CYS	1228	34.717	15.869	-3.705	1.00	16.56
ATOM	5364	N	VAL	1229	38.321	16.140	-3.578	1.00	18.38
ATOM	5365	CA	VAL	1229	39.012	16.545	-2.355	1.00	18.01
ATOM	5366	CB	VAL	1229	39.862	15.384	-1.726	1.00	10.45
ATOM	5367	CG1	VAL	1229	40.789	15.931	-0.620	1.00	11.88
ATOM	5368	CG2	VAL	1229	38.951	14.329	-1.141	1.00	13.18
ATOM	5369	C	VAL	1229	39.904	17.751	-2.630	1.00	19.38
ATOM	5370	O	VAL	1229	40.005	18.657	-1.795	1.00	18.20
ATOM	5371	N	THR	1230	40.536	17.764	-3.805	1.00	17.44
ATOM	5372	CA	THR	1230	41.401	18.864	-4.201	1.00	17.69
ATOM	5373	CB	THR	1230	42.092	18.554	-5.530	1.00	19.95
ATOM	5374	OG1	THR	1230	43.054	17.510	-5.331	1.00	21.23
ATOM	5375	CG2	THR	1230	42.787	19.782	-6.060	1.00	15.76
ATOM	5376	C	THR	1230	40.606	20.166	-4.290	1.00	15.19
ATOM	5377	O	THR	1230	41.119	21.241	-3.987	1.00	13.68
ATOM	5378	N	ASN	1231	39.332	20.043	-4.638	1.00	12.63
ATOM	5379	CA	ASN	1231	38.438	21.179	-4.733	1.00	17.77
ATOM	5380	CB	ASN	1231	37.264	20.845	-5.649	1.00	19.66
ATOM	5381	CG	ASN	1231	37.690	20.658	-7.063	1.00	22.77
ATOM	5382	OD1	ASN	1231	38.738	21.157	-7.490	1.00	22.53
ATOM	5383	ND2	ASN	1231	36.906	19.909	-7.804	1.00	23.03
ATOM	5384	C	ASN	1231	37.893	21.616	-3.381	1.00	16.56
ATOM	5385	O	ASN	1231	37.706	22.816	-3.144	1.00	16.23
ATOM	5386	N	LEU	1232	37.551	20.648	-2.530	1.00	14.26
ATOM	5387	CA	LEU	1232	37.039	20.932	-1.185	1.00	12.02
ATOM	5388	CB	LEU	1232	36.498	19.659	-0.532	1.00	10.33
ATOM	5389	CG	LEU	1232	35.136	19.256	-1.098	1.00	7.35

Figure 23.35

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ATOM	5390	CD1	LEU	1232	34.702	17.857	-0.664	1.00	6.30
ATOM	5391	CD2	LEU	1232	34.112	20.293	-0.685	1.00	8.09
ATOM	5392	C	LEU	1232	38.140	21.583	-0.354	1.00	10.60
ATOM	5393	O	LEU	1232	37.876	22.440	0.468	1.00	13.90
ATOM	5394	N	GLN	1233	39.381	21.211	-0.619	1.00	9.40
ATOM	5395	CA	GLN	1233	40.527	21.802	0.047	1.00	10.95
ATOM	5396	CB	GLN	1233	41.813	21.154	-0.451	1.00	12.59
ATOM	5397	CG	GLN	1233	43.082	21.692	0.186	1.00	11.94
ATOM	5398	CD	GLN	1233	43.454	20.944	1.459	1.00	20.32
ATOM	5399	OE1	GLN	1233	43.579	19.711	1.456	1.00	14.32
ATOM	5400	NE2	GLN	1233	43.636	21.685	2.554	1.00	14.79
ATOM	5401	C	GLN	1233	40.602	23.299	-0.253	1.00	14.74
ATOM	5402	O	GLN	1233	41.013	24.089	0.600	1.00	18.19
ATOM	5403	N	GLU	1234	40.254	23.687	-1.478	1.00	11.85
ATOM	5404	CA	GLU	1234	40.292	25.103	-1.861	1.00	10.69
ATOM	5405	CB	GLU	1234	40.254	25.266	-3.394	1.00	10.20
ATOM	5406	CG	GLU	1234	40.109	26.712	-3.907	1.00	2.85
ATOM	5407	CD	GLU	1234	41.343	27.573	-3.712	1.00	8.95
ATOM	5408	OE1	GLU	1234	42.384	27.075	-3.232	1.00	18.14
ATOM	5409	OE2	GLU	1234	41.286	28.772	-4.064	1.00	19.71
ATOM	5410	C	GLU	1234	39.113	25.807	-1.200	1.00	6.36
ATOM	5411	O	GLU	1234	39.244	26.914	-0.730	1.00	10.88
ATOM	5412	N	VAL	1235	37.962	25.155	-1.203	1.00	3.91
ATOM	5413	CA	VAL	1235	36.761	25.678	-0.564	1.00	7.66
ATOM	5414	CB	VAL	1235	35.588	24.663	-0.643	1.00	5.62
ATOM	5415	CG1	VAL	1235	34.394	25.122	0.173	1.00	4.56
ATOM	5416	CG2	VAL	1235	35.156	24.485	-2.073	1.00	9.28
ATOM	5417	C	VAL	1235	37.070	25.958	0.911	1.00	14.57
ATOM	5418	O	VAL	1235	36.624	26.970	1.463	1.00	14.73
ATOM	5419	N	ALA	1236	37.823	25.048	1.537	1.00	15.81
ATOM	5420	CA	ALA	1236	38.208	25.167	2.945	1.00	13.64
ATOM	5421	CB	ALA	1236	38.887	23.873	3.445	1.00	6.15
ATOM	5422	C	ALA	1236	39.131	26.369	3.118	1.00	15.64
ATOM	5423	O	ALA	1236	38.976	27.142	4.077	1.00	14.87
ATOM	5424	N	ARG	1237	40.054	26.535	2.165	1.00	9.14
ATOM	5425	CA	ARG	1237	40.984	27.660	2.167	1.00	8.25
ATOM	5426	CB	ARG	1237	42.032	27.507	1.061	1.00	8.87
ATOM	5427	CG	ARG	1237	43.146	28.542	1.170	1.00	11.40
ATOM	5428	CD	ARG	1237	43.929	28.662	-0.128	1.00	5.48
ATOM	5429	NE	ARG	1237	43.041	29.142	-1.171	1.00	9.71
ATOM	5430	CZ	ARG	1237	42.742	30.422	-1.340	1.00	13.92
ATOM	5431	NH1	ARG	1237	43.281	31.332	-0.541	1.00	11.41
ATOM	5432	NH2	ARG	1237	41.859	30.793	-2.258	1.00	15.76
ATOM	5433	C	ARG	1237	40.258	29.014	1.997	1.00	9.36
ATOM	5434	O	ARG	1237	40.513	29.973	2.727	1.00	9.20
ATOM	5435	N	ILE	1238	39.340	29.067	1.049	1.00	7.45
ATOM	5436	CA	ILE	1238	38.591	30.270	0.767	1.00	10.86
ATOM	5437	CB	ILE	1238	37.764	30.092	-0.536	1.00	11.86
ATOM	5438	CG2	ILE	1238	36.747	31.231	-0.685	1.00	11.72
ATOM	5439	CG1	ILE	1238	38.700	29.983	-1.746	1.00	8.57
ATOM	5440	CD1	ILE	1238	37.977	29.666	-3.054	1.00	9.38
ATOM	5441	C	ILE	1238	37.659	30.702	1.908	1.00	11.50
ATOM	5442	O	ILE	1238	37.569	31.891	2.230	1.00	11.72
ATOM	5443	N	VAL	1239	36.951	29.736	2.496	1.00	11.77
ATOM	5444	CA	VAL	1239	36.006	29.989	3.576	1.00	9.26
ATOM	5445	CB	VAL	1239	35.048	28.771	3.746	1.00	6.63
ATOM	5446	CG1	VAL	1239	34.264	28.852	5.020	1.00	8.44
ATOM	5447	CG2	VAL	1239	34.075	28.739	2.602	1.00	5.57
ATOM	5448	C	VAL	1239	36.663	30.388	4.899	1.00	14.36
ATOM	5449	O	VAL	1239	36.249	31.365	5.540	1.00	15.36

Figure 23.36

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ATOM	5450	N	GLY	1240	37.753	29.720	5.263	1.00	14.01
ATOM	5451	CA	GLY	1240	38.368	30.053	6.524	1.00	9.80
ATOM	5452	C	GLY	1240	39.828	30.403	6.608	1.00	13.00
ATOM	5453	O	GLY	1240	40.313	30.636	7.696	1.00	17.82
ATOM	5454	N	ASN	1241	40.554	30.413	5.504	1.00	11.91
ATOM	5455	CA	ASN	1241	41.979	30.736	5.555	1.00	14.24
ATOM	5456	CB	ASN	1241	42.822	29.557	5.082	1.00	19.51
ATOM	5457	CG	ASN	1241	42.800	28.373	6.026	1.00	29.10
ATOM	5458	OD1	ASN	1241	43.763	27.624	6.061	1.00	31.42
ATOM	5459	ND2	ASN	1241	41.675	28.117	6.680	1.00	32.93
ATOM	5460	C	ASN	1241	42.339	31.863	4.623	1.00	16.45
ATOM	5461	O	ASN	1241	43.506	32.027	4.292	1.00	21.90
ATOM	5462	N	SER	1242	41.378	32.658	4.199	1.00	15.33
ATOM	5463	CA	SER	1242	41.734	33.694	3.250	1.00	15.25
ATOM	5464	CB	SER	1242	41.006	33.440	1.934	1.00	15.60
ATOM	5465	OG	SER	1242	39.599	33.389	2.121	1.00	22.94
ATOM	5466	C	SER	1242	41.500	35.116	3.697	1.00	14.71
ATOM	5467	O	SER	1242	41.797	36.057	2.953	1.00	16.28
ATOM	5468	N	GLY	1243	40.960	35.282	4.898	1.00	12.92
ATOM	5469	CA	GLY	1243	40.693	36.616	5.400	1.00	9.53
ATOM	5470	C	GLY	1243	39.217	36.932	5.565	1.00	9.01
ATOM	5471	O	GLY	1243	38.864	38.027	6.002	1.00	11.50
ATOM	5472	N	LEU	1244	38.357	36.003	5.169	1.00	5.30
ATOM	5473	CA	LEU	1244	36.920	36.175	5.315	1.00	5.96
ATOM	5474	CB	LEU	1244	36.152	35.249	4.355	1.00	6.98
ATOM	5475	CG	LEU	1244	35.998	35.540	2.861	1.00	7.31
ATOM	5476	CD1	LEU	1244	35.190	34.413	2.255	1.00	2.00
ATOM	5477	CD2	LEU	1244	35.281	36.871	2.632	1.00	5.17
ATOM	5478	C	LEU	1244	36.562	35.796	6.747	1.00	8.96
ATOM	5479	O	LEU	1244	37.274	35.012	7.372	1.00	7.08
ATOM	5480	N	ASN	1245	35.472	36.351	7.267	1.00	9.02
ATOM	5481	CA	ASN	1245	35.024	36.037	8.612	1.00	6.86
ATOM	5482	CB	ASN	1245	34.405	37.279	9.256	1.00	11.52
ATOM	5483	CG	ASN	1245	34.123	37.101	10.735	1.00	6.02
ATOM	5484	OD1	ASN	1245	33.785	36.020	11.221	1.00	7.40
ATOM	5485	ND2	ASN	1245	34.203	38.195	11.449	1.00	9.26
ATOM	5486	C	ASN	1245	34.007	34.917	8.558	1.00	3.99
ATOM	5487	O	ASN	1245	32.868	35.128	8.209	1.00	8.16
ATOM	5488	N	ILE	1246	34.424	33.722	8.941	1.00	5.99
ATOM	5489	CA	ILE	1246	33.545	32.550	8.927	1.00	7.78
ATOM	5490	CB	ILE	1246	34.368	31.274	9.265	1.00	12.12
ATOM	5491	CG2	ILE	1246	34.591	31.154	10.780	1.00	11.09
ATOM	5492	CG1	ILE	1246	33.671	30.038	8.720	1.00	9.96
ATOM	5493	CD1	ILE	1246	34.515	28.748	8.879	1.00	6.32
ATOM	5494	C	ILE	1246	32.300	32.677	9.824	1.00	6.28
ATOM	5495	O	ILE	1246	31.308	31.963	9.655	1.00	11.95
ATOM	5496	N	TYR	1247	32.326	33.626	10.750	1.00	9.19
ATOM	5497	CA	TYR	1247	31.193	33.857	11.658	1.00	10.80
ATOM	5498	CB	TYR	1247	31.671	34.354	13.035	1.00	12.62
ATOM	5499	CG	TYR	1247	32.213	33.282	13.947	1.00	7.47
ATOM	5500	CD1	TYR	1247	32.224	31.943	13.561	1.00	13.13
ATOM	5501	CE1	TYR	1247	32.712	30.950	14.409	1.00	12.41
ATOM	5502	CD2	TYR	1247	32.699	33.607	15.199	1.00	12.52
ATOM	5503	CE2	TYR	1247	33.174	32.645	16.049	1.00	13.50
ATOM	5504	CZ	TYR	1247	33.183	31.315	15.657	1.00	16.73
ATOM	5505	OH	TYR	1247	33.667	30.366	16.517	1.00	12.14
ATOM	5506	C	TYR	1247	30.195	34.871	11.133	1.00	5.74
ATOM	5507	O	TYR	1247	29.082	34.965	11.648	1.00	6.91
ATOM	5508	N	ASN	1248	30.610	35.650	10.144	1.00	4.94
ATOM	5509	CA	ASN	1248	29.760	36.688	9.584	1.00	7.73

Figure 23.37

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ATOM	5510	CB	ASN	1248	29.731	37.912	10.511	1.00	4.05
ATOM	5511	CG	ASN	1248	28.605	38.880	10.166	1.00	6.16
ATOM	5512	OD1	ASN	1248	28.290	39.109	8.994	1.00	15.77
ATOM	5513	ND2	ASN	1248	27.980	39.434	11.185	1.00	5.24
ATOM	5514	C	ASN	1248	30.410	37.059	8.280	1.00	7.26
ATOM	5515	O	ASN	1248	31.371	37.810	8.269	1.00	4.31
ATOM	5516	N	LEU	1249	29.888	36.509	7.190	1.00	11.85
ATOM	5517	CA	LEU	1249	30.458	36.745	5.859	1.00	9.40
ATOM	5518	CB	LEU	1249	29.570	36.123	4.784	1.00	7.40
ATOM	5519	CG	LEU	1249	30.016	36.277	3.329	1.00	4.43
ATOM	5520	CD1	LEU	1249	31.446	35.883	3.137	1.00	2.00
ATOM	5521	CD2	LEU	1249	29.133	35.405	2.479	1.00	2.74
ATOM	5522	C	LEU	1249	30.660	38.195	5.520	1.00	5.20
ATOM	5523	O	LEU	1249	31.690	38.560	4.965	1.00	7.99
ATOM	5524	N	TYR	1250	29.692	39.006	5.938	1.00	4.98
ATOM	5525	CA	TYR	1250	29.639	40.434	5.674	1.00	5.76
ATOM	5526	CB	TYR	1250	28.182	40.823	5.420	1.00	2.18
ATOM	5527	CG	TYR	1250	27.555	39.939	4.378	1.00	4.32
ATOM	5528	CD1	TYR	1250	26.485	39.096	4.697	1.00	5.22
ATOM	5529	CE1	TYR	1250	25.987	38.174	3.767	1.00	6.53
ATOM	5530	CD2	TYR	1250	28.108	39.862	3.096	1.00	2.53
ATOM	5531	CE2	TYR	1250	27.612	38.962	2.164	1.00	4.06
ATOM	5532	CZ	TYR	1250	26.554	38.117	2.502	1.00	5.21
ATOM	5533	OH	TYR	1250	26.039	37.250	1.550	1.00	6.66
ATOM	5534	C	TYR	1250	30.248	41.368	6.704	1.00	6.45
ATOM	5535	O	TYR	1250	29.915	42.544	6.742	1.00	9.74
ATOM	5536	N	ALA	1251	31.164	40.867	7.513	1.00	4.85
ATOM	5537	CA	ALA	1251	31.809	41.699	8.508	1.00	5.28
ATOM	5538	CB	ALA	1251	31.428	41.228	9.913	1.00	6.54
ATOM	5539	C	ALA	1251	33.299	41.585	8.292	1.00	6.33
ATOM	5540	O	ALA	1251	33.755	40.686	7.600	1.00	7.76
ATOM	5541	N	PRO	1252	34.074	42.555	8.779	1.00	5.83
ATOM	5542	CD	PRO	1252	33.646	43.807	9.421	1.00	3.26
ATOM	5543	CA	PRO	1252	35.529	42.511	8.628	1.00	7.99
ATOM	5544	CB	PRO	1252	35.969	43.880	9.141	1.00	10.32
ATOM	5545	CG	PRO	1252	34.901	44.222	10.123	1.00	7.37
ATOM	5546	C	PRO	1252	36.076	41.412	9.531	1.00	10.99
ATOM	5547	O	PRO	1252	35.388	40.962	10.448	1.00	14.28
ATOM	5548	N	CYS	1253	37.295	40.966	9.275	1.00	6.80
ATOM	5549	CA	CYS	1253	37.889	39.946	10.101	1.00	14.69
ATOM	5550	C	CYS	1253	38.878	40.622	11.006	1.00	16.65
ATOM	5551	O	CYS	1253	39.835	41.225	10.523	1.00	19.87
ATOM	5552	CB	CYS	1253	38.621	38.917	9.257	1.00	13.74
ATOM	5553	SG	CYS	1253	39.432	37.601	10.228	1.00	14.76
ATOM	5554	N	ALA	1254	38.632	40.548	12.311	1.00	21.14
ATOM	5555	CA	ALA	1254	39.535	41.137	13.297	1.00	26.99
ATOM	5556	CB	ALA	1254	38.973	40.974	14.708	1.00	28.81
ATOM	5557	C	ALA	1254	40.897	40.470	13.199	1.00	29.08
ATOM	5558	O	ALA	1254	41.044	39.297	13.538	1.00	29.33
ATOM	5559	N	GLY	1255	41.890	41.243	12.757	1.00	34.01
ATOM	5560	CA	GLY	1255	43.243	40.725	12.592	1.00	35.60
ATOM	5561	C	GLY	1255	43.283	39.675	11.498	1.00	40.58
ATOM	5562	O	GLY	1255	43.736	38.545	11.711	1.00	38.65
ATOM	5563	N	GLY	1256	42.813	40.082	10.319	1.00	45.16
ATOM	5564	CA	GLY	1256	42.728	39.217	9.161	1.00	46.61
ATOM	5565	C	GLY	1256	44.009	38.751	8.513	1.00	47.23
ATOM	5566	O	GLY	1256	44.878	39.528	8.119	1.00	49.78
ATOM	5567	N	VAL	1257	44.070	37.441	8.358	1.00	46.33
ATOM	5568	CA	VAL	1257	45.166	36.739	7.737	1.00	43.27
ATOM	5569	CB	VAL	1257	45.393	35.372	8.440	1.00	45.53

Figure 23.38

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ATOM	5570	CG1	VAL	1257	45.960	35.566	9.829	1.00	42.90
ATOM	5571	CG2	VAL	1257	44.074	34.555	8.447	1.00	45.07
ATOM	5572	C	VAL	1257	44.715	36.379	6.330	1.00	42.32
ATOM	5573	O	VAL	1257	43.853	37.033	5.751	1.00	39.41
ATOM	5574	N	PRO	1258	45.473	35.490	5.701	1.00	43.56
ATOM	5575	CD	PRO	1258	46.844	36.015	5.847	1.00	43.04
ATOM	5576	CA	PRO	1258	45.401	34.849	4.384	1.00	42.07
ATOM	5577	CB	PRO	1258	46.311	35.738	3.519	1.00	41.83
ATOM	5578	CG	PRO	1258	47.013	36.723	4.546	1.00	43.18
ATOM	5579	C	PRO	1258	46.069	33.501	4.673	1.00	40.51
ATOM	5580	O	PRO	1258	46.868	32.988	3.866	1.00	39.55
ATOM	5581	N	SER	1259	45.794	32.972	5.871	1.00	37.33
ATOM	5582	CA	SER	1259	46.406	31.721	6.287	1.00	30.52
ATOM	5583	CB	SER	1259	47.780	32.011	6.875	1.00	28.60
ATOM	5584	OG	SER	1259	48.547	30.830	6.936	1.00	26.07
ATOM	5585	C	SER	1259	45.587	30.930	7.291	1.00	26.46
ATOM	5586	O	SER	1259	44.493	31.340	7.668	1.00	21.66
ATOM	5587	N	HIS	1260	46.125	29.771	7.678	1.00	25.96
ATOM	5588	CA	HIS	1260	45.491	28.870	8.647	1.00	26.85
ATOM	5589	CB	HIS	1260	45.664	27.384	8.242	1.00	21.97
ATOM	5590	CG	HIS	1260	47.066	27.001	7.873	1.00	19.08
ATOM	5591	CD2	HIS	1260	47.757	27.151	6.717	1.00	15.25
ATOM	5592	ND1	HIS	1260	47.939	26.417	8.764	1.00	19.30
ATOM	5593	CE1	HIS	1260	49.109	26.229	8.176	1.00	17.01
ATOM	5594	NE2	HIS	1260	49.025	26.666	6.933	1.00	17.36
ATOM	5595	C	HIS	1260	45.958	29.102	10.107	1.00	28.23
ATOM	5596	O	HIS	1260	45.543	28.378	11.036	1.00	27.81
ATOM	5597	N	PHE	1261	46.834	30.098	10.286	1.00	29.65
ATOM	5598	CA	PHE	1261	47.374	30.495	11.599	1.00	25.59
ATOM	5599	CB	PHE	1261	48.523	29.568	12.052	1.00	22.38
ATOM	5600	CG	PHE	1261	49.845	29.865	11.388	1.00	17.76
ATOM	5601	CD1	PHE	1261	50.843	30.591	12.058	1.00	20.02
ATOM	5602	CD2	PHE	1261	50.057	29.511	10.054	1.00	14.74
ATOM	5603	CE1	PHE	1261	52.026	30.970	11.400	1.00	18.59
ATOM	5604	CE2	PHE	1261	51.247	29.893	9.392	1.00	15.00
ATOM	5605	CZ	PHE	1261	52.228	30.626	10.074	1.00	16.38
ATOM	5606	C	PHE	1261	47.903	31.929	11.481	1.00	26.14
ATOM	5607	O	PHE	1261	47.963	32.485	10.373	1.00	25.58
ATOM	5608	N	ARG	1262	48.323	32.491	12.616	1.00	26.52
ATOM	5609	CA	ARG	1262	48.907	33.826	12.674	1.00	27.43
ATOM	5610	CB	ARG	1262	47.858	34.922	12.618	1.00	28.18
ATOM	5611	CG	ARG	1262	46.954	34.994	13.822	1.00	26.50
ATOM	5612	CD	ARG	1262	45.915	36.056	13.593	1.00	30.63
ATOM	5613	NE	ARG	1262	44.985	36.203	14.709	1.00	31.92
ATOM	5614	CZ	ARG	1262	45.153	37.050	15.724	1.00	31.48
ATOM	5615	NH1	ARG	1262	46.233	37.831	15.779	1.00	32.38
ATOM	5616	NH2	ARG	1262	44.205	37.149	16.655	1.00	32.05
ATOM	5617	C	ARG	1262	49.690	33.964	13.955	1.00	28.74
ATOM	5618	O	ARG	1262	49.492	33.203	14.903	1.00	29.44
ATOM	5619	N	TYR	1263	50.626	34.898	13.952	1.00	29.68
ATOM	5620	CA	TYR	1263	51.459	35.158	15.118	1.00	31.09
ATOM	5621	CB	TYR	1263	52.936	35.303	14.714	1.00	30.06
ATOM	5622	CG	TYR	1263	53.561	34.069	14.077	1.00	33.51
ATOM	5623	CD1	TYR	1263	53.994	34.094	12.746	1.00	32.99
ATOM	5624	CE1	TYR	1263	54.602	32.978	12.155	1.00	28.92
ATOM	5625	CD2	TYR	1263	53.752	32.891	14.803	1.00	30.89
ATOM	5626	CE2	TYR	1263	54.361	31.772	14.217	1.00	29.84
ATOM	5627	CZ	TYR	1263	54.780	31.833	12.897	1.00	30.19
ATOM	5628	OH	TYR	1263	55.396	30.757	12.333	1.00	29.21
ATOM	5629	C	TYR	1263	50.970	36.447	15.773	1.00	31.03

Figure 23.39

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ATOM	5630	O	TYR	1263	50.470	37.367	15.105	1.00	30.95
ATOM	5631	N	GLU	1264	51.101	36.498	17.087	1.00	31.38
ATOM	5632	CA	GLU	1264	50.697	37.659	17.858	1.00	33.42
ATOM	5633	CB	GLU	1264	49.425	37.348	18.616	1.00	37.16
ATOM	5634	CG	GLU	1264	48.819	38.532	19.300	1.00	38.61
ATOM	5635	CD	GLU	1264	47.972	38.098	20.447	1.00	40.14
ATOM	5636	OE1	GLU	1264	46.765	38.419	20.435	1.00	37.96
ATOM	5637	OE2	GLU	1264	48.521	37.413	21.344	1.00	40.00
ATOM	5638	C	GLU	1264	51.872	37.839	18.802	1.00	35.26
ATOM	5639	O	GLU	1264	51.917	37.271	19.898	1.00	34.94
ATOM	5640	N	LYS	1265	52.817	38.646	18.335	1.00	39.89
ATOM	5641	CA	LYS	1265	54.079	38.897	19.004	1.00	41.43
ATOM	5642	CB	LYS	1265	53.931	39.220	20.499	1.00	46.86
ATOM	5643	CG	LYS	1265	55.293	39.473	21.147	1.00	54.76
ATOM	5644	CD	LYS	1265	55.199	40.190	22.479	1.00	59.45
ATOM	5645	CE	LYS	1265	56.439	41.053	22.707	1.00	60.55
ATOM	5646	NZ	LYS	1265	57.713	40.287	22.592	1.00	65.22
ATOM	5647	C	LYS	1265	54.809	37.579	18.792	1.00	39.32
ATOM	5648	O	LYS	1265	55.228	37.283	17.667	1.00	39.75
ATOM	5649	N	ASP	1266	54.860	36.740	19.820	1.00	37.46
ATOM	5650	CA	ASP	1266	55.542	35.462	19.700	1.00	32.74
ATOM	5651	CB	ASP	1266	56.882	35.517	20.424	1.00	31.42
ATOM	5652	CG	ASP	1266	57.912	36.369	19.658	1.00	20.00
ATOM	5653	OD1	ASP	1266	57.544	37.044	18.652	1.00	20.00
ATOM	5654	OD2	ASP	1266	59.114	36.349	20.039	1.00	20.00
ATOM	5655	C	ASP	1266	54.701	34.274	20.130	1.00	28.07
ATOM	5656	O	ASP	1266	55.205	33.261	20.607	1.00	32.14
ATOM	5657	N	THR	1267	53.401	34.438	19.968	1.00	22.25
ATOM	5658	CA	THR	1267	52.437	33.402	20.280	1.00	22.63
ATOM	5659	CB	THR	1267	51.296	33.938	21.194	1.00	19.80
ATOM	5660	OG1	THR	1267	51.811	34.179	22.507	1.00	20.60
ATOM	5661	CG2	THR	1267	50.141	32.939	21.283	1.00	15.20
ATOM	5662	C	THR	1267	51.812	32.965	18.971	1.00	22.93
ATOM	5663	O	THR	1267	51.497	33.798	18.115	1.00	24.18
ATOM	5664	N	VAL	1268	51.705	31.660	18.779	1.00	21.75
ATOM	5665	CA	VAL	1268	51.060	31.164	17.584	1.00	17.51
ATOM	5666	CB	VAL	1268	51.491	29.733	17.234	1.00	18.64
ATOM	5667	CG1	VAL	1268	50.955	29.361	15.842	1.00	18.22
ATOM	5668	CG2	VAL	1268	53.000	29.619	17.285	1.00	17.56
ATOM	5669	C	VAL	1268	49.585	31.146	17.958	1.00	14.97
ATOM	5670	O	VAL	1268	49.216	30.577	18.992	1.00	16.77
ATOM	5671	N	VAL	1269	48.761	31.826	17.166	1.00	14.64
ATOM	5672	CA	VAL	1269	47.342	31.870	17.414	1.00	12.95
ATOM	5673	CB	VAL	1269	46.793	33.307	17.290	1.00	6.85
ATOM	5674	CG1	VAL	1269	45.367	33.343	17.747	1.00	3.93
ATOM	5675	CG2	VAL	1269	47.615	34.264	18.110	1.00	3.36
ATOM	5676	C	VAL	1269	46.666	30.967	16.378	1.00	16.47
ATOM	5677	O	VAL	1269	46.794	31.180	15.166	1.00	15.98
ATOM	5678	N	VAL	1270	45.997	29.929	16.864	1.00	13.62
ATOM	5679	CA	VAL	1270	45.289	28.980	16.026	1.00	13.96
ATOM	5680	CB	VAL	1270	45.590	27.555	16.487	1.00	9.13
ATOM	5681	CG1	VAL	1270	44.584	26.581	15.913	1.00	15.74
ATOM	5682	CG2	VAL	1270	46.984	27.186	16.034	1.00	8.89
ATOM	5683	C	VAL	1270	43.808	29.313	16.157	1.00	14.66
ATOM	5684	O	VAL	1270	43.351	29.597	17.264	1.00	17.62
ATOM	5685	N	GLN	1271	43.050	29.286	15.056	1.00	13.61
ATOM	5686	CA	GLN	1271	41.633	29.664	15.125	1.00	11.49
ATOM	5687	CB	GLN	1271	41.466	31.087	14.591	1.00	12.08
ATOM	5688	CG	GLN	1271	42.238	32.063	15.437	1.00	13.81
ATOM	5689	CD	GLN	1271	42.309	33.420	14.848	1.00	16.51

Figure 23.40

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ATOM	5690	OE1	GLN	1271	43.104	33.656	13.949	1.00	23.31
ATOM	5691	NE2	GLN	1271	41.474	34.346	15.344	1.00	11.91
ATOM	5692	C	GLN	1271	40.644	28.720	14.482	1.00	11.75
ATOM	5693	O	GLN	1271	39.492	29.087	14.202	1.00	14.11
ATOM	5694	N	ASP	1272	41.088	27.474	14.342	1.00	14.05
ATOM	5695	CA	ASP	1272	40.301	26.398	13.761	1.00	10.19
ATOM	5696	CB	ASP	1272	41.181	25.589	12.799	1.00	14.03
ATOM	5697	CG	ASP	1272	40.444	24.412	12.154	1.00	13.51
ATOM	5698	OD1	ASP	1272	39.203	24.305	12.256	1.00	20.46
ATOM	5699	OD2	ASP	1272	41.126	23.571	11.541	1.00	24.72
ATOM	5700	C	ASP	1272	39.875	25.535	14.923	1.00	9.82
ATOM	5701	O	ASP	1272	40.695	24.843	15.483	1.00	12.05
ATOM	5702	N	LEU	1273	38.588	25.543	15.242	1.00	6.07
ATOM	5703	CA	LEU	1273	38.058	24.790	16.365	1.00	10.92
ATOM	5704	CB	LEU	1273	36.845	25.509	16.951	1.00	5.16
ATOM	5705	CG	LEU	1273	37.019	26.976	17.328	1.00	6.05
ATOM	5706	CD1	LEU	1273	35.755	27.440	18.001	1.00	4.65
ATOM	5707	CD2	LEU	1273	38.181	27.165	18.226	1.00	7.00
ATOM	5708	C	LEU	1273	37.748	23.319	16.088	1.00	13.09
ATOM	5709	O	LEU	1273	37.129	22.636	16.922	1.00	10.63
ATOM	5710	N	GLY	1274	38.196	22.876	14.903	1.00	13.95
ATOM	5711	CA	GLY	1274	38.070	21.504	14.414	1.00	12.07
ATOM	5712	C	GLY	1274	36.725	20.852	14.204	1.00	12.36
ATOM	5713	O	GLY	1274	36.622	19.632	14.336	1.00	13.37
ATOM	5714	N	ASN	1275	35.708	21.618	13.823	1.00	9.66
ATOM	5715	CA	ASN	1275	34.383	21.034	13.644	1.00	9.00
ATOM	5716	CB	ASN	1275	33.334	21.832	14.429	1.00	11.33
ATOM	5717	CG	ASN	1275	33.670	21.963	15.895	1.00	15.82
ATOM	5718	OD1	ASN	1275	33.934	20.977	16.579	1.00	17.09
ATOM	5719	ND2	ASN	1275	33.675	23.191	16.387	1.00	10.47
ATOM	5720	C	ASN	1275	33.906	20.941	12.201	1.00	9.66
ATOM	5721	O	ASN	1275	32.873	20.343	11.927	1.00	9.68
ATOM	5722	N	ILE	1276	34.691	21.489	11.286	1.00	9.97
ATOM	5723	CA	ILE	1276	34.307	21.568	9.877	1.00	11.82
ATOM	5724	CB	ILE	1276	34.343	23.084	9.423	1.00	11.44
ATOM	5725	CG2	ILE	1276	34.040	23.248	7.951	1.00	10.15
ATOM	5726	CG1	ILE	1276	33.346	23.886	10.264	1.00	9.40
ATOM	5727	CD1	ILE	1276	33.562	25.376	10.229	1.00	2.81
ATOM	5728	C	ILE	1276	35.232	20.737	9.001	1.00	9.96
ATOM	5729	O	ILE	1276	36.454	20.768	9.192	1.00	7.64
ATOM	5730	N	PHE	1277	34.633	19.971	8.077	1.00	14.17
ATOM	5731	CA	PHE	1277	35.362	19.109	7.122	1.00	13.77
ATOM	5732	CB	PHE	1277	36.213	19.970	6.145	1.00	11.84
ATOM	5733	CG	PHE	1277	35.386	20.878	5.232	1.00	13.15
ATOM	5734	CD1	PHE	1277	35.796	22.188	4.963	1.00	12.93
ATOM	5735	CD2	PHE	1277	34.203	20.419	4.640	1.00	14.08
ATOM	5736	CE1	PHE	1277	35.043	23.027	4.113	1.00	13.33
ATOM	5737	CE2	PHE	1277	33.449	21.252	3.792	1.00	9.73
ATOM	5738	CZ	PHE	1277	33.879	22.559	3.530	1.00	12.32
ATOM	5739	C	PHE	1277	36.236	18.076	7.843	1.00	11.52
ATOM	5740	O	PHE	1277	37.285	17.660	7.340	1.00	10.20
ATOM	5741	N	THR	1278	35.768	17.624	9.003	1.00	11.71
ATOM	5742	CA	THR	1278	36.526	16.653	9.807	1.00	14.47
ATOM	5743	CB	THR	1278	35.859	16.413	11.188	1.00	12.43
ATOM	5744	OG1	THR	1278	34.504	15.983	10.997	1.00	5.40
ATOM	5745	CG2	THR	1278	35.858	17.670	12.011	1.00	14.30
ATOM	5746	C	THR	1278	36.702	15.289	9.129	1.00	16.87
ATOM	5747	O	THR	1278	37.726	14.624	9.333	1.00	21.05
ATOM	5748	N	ARG	1279	35.709	14.896	8.326	1.00	14.96
ATOM	5749	CA	ARG	1279	35.703	13.614	7.631	1.00	15.72

Figure 23.41

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ATOM	5750	CB	ARG	1279	34.276	13.103	7.475	1.00	10.95
ATOM	5751	CG	ARG	1279	33.664	12.659	8.766	1.00	17.88
ATOM	5752	CD	ARG	1279	34.529	11.595	9.377	1.00	17.45
ATOM	5753	NE	ARG	1279	34.157	11.334	10.757	1.00	25.93
ATOM	5754	CZ	ARG	1279	34.196	10.135	11.327	1.00	31.46
ATOM	5755	NH1	ARG	1279	34.587	9.072	10.631	1.00	34.18
ATOM	5756	NH2	ARG	1279	33.875	10.000	12.605	1.00	35.30
ATOM	5757	C	ARG	1279	36.362	13.607	6.275	1.00	15.10
ATOM	5758	O	ARG	1279	36.410	12.563	5.623	1.00	17.91
ATOM	5759	N	LEU	1280	36.900	14.746	5.863	1.00	14.43
ATOM	5760	CA	LEU	1280	37.543	14.846	4.574	1.00	12.87
ATOM	5761	CB	LEU	1280	37.341	16.230	3.937	1.00	12.66
ATOM	5762	CG	LEU	1280	35.919	16.555	3.482	1.00	11.37
ATOM	5763	CD1	LEU	1280	35.851	17.965	2.842	1.00	12.24
ATOM	5764	CD2	LEU	1280	35.456	15.453	2.519	1.00	10.36
ATOM	5765	C	LEU	1280	38.993	14.615	4.736	1.00	12.38
ATOM	5766	O	LEU	1280	39.582	15.120	5.671	1.00	11.84
ATOM	5767	N	PRO	1281	39.603	13.847	3.815	1.00	13.92
ATOM	5768	CD	PRO	1281	38.987	13.063	2.725	1.00	9.83
ATOM	5769	CA	PRO	1281	41.037	13.588	3.913	1.00	14.25
ATOM	5770	CB	PRO	1281	41.240	12.413	2.960	1.00	15.39
ATOM	5771	CG	PRO	1281	40.184	12.630	1.920	1.00	12.69
ATOM	5772	C	PRO	1281	41.828	14.813	3.468	1.00	17.51
ATOM	5773	O	PRO	1281	42.659	14.718	2.569	1.00	21.78
ATOM	5774	N	LEU	1282	41.589	15.952	4.115	1.00	16.38
ATOM	5775	CA	LEU	1282	42.273	17.185	3.769	1.00	13.89
ATOM	5776	CB	LEU	1282	41.417	18.390	4.201	1.00	15.96
ATOM	5777	CG	LEU	1282	40.001	18.593	3.637	1.00	15.64
ATOM	5778	CD1	LEU	1282	39.424	19.886	4.192	1.00	9.38
ATOM	5779	CD2	LEU	1282	39.973	18.602	2.108	1.00	11.12
ATOM	5780	C	LEU	1282	43.689	17.315	4.354	1.00	15.19
ATOM	5781	O	LEU	1282	44.111	16.514	5.177	1.00	18.07
ATOM	5782	N	LYS	1283	44.466	18.252	3.828	1.00	15.73
ATOM	5783	CA	LYS	1283	45.795	18.500	4.355	1.00	15.07
ATOM	5784	CB	LYS	1283	46.727	18.996	3.272	1.00	14.37
ATOM	5785	CG	LYS	1283	46.940	18.014	2.179	1.00	19.99
ATOM	5786	CD	LYS	1283	48.122	18.437	1.340	1.00	24.07
ATOM	5787	CE	LYS	1283	47.688	18.943	-0.014	1.00	30.06
ATOM	5788	NZ	LYS	1283	48.865	19.337	-0.841	1.00	36.72
ATOM	5789	C	LYS	1283	45.564	19.601	5.369	1.00	17.48
ATOM	5790	O	LYS	1283	44.858	20.563	5.078	1.00	19.13
ATOM	5791	N	ARG	1284	46.140	19.456	6.555	1.00	17.51
ATOM	5792	CA	ARG	1284	45.957	20.418	7.630	1.00	15.14
ATOM	5793	CB	ARG	1284	44.941	19.890	8.652	1.00	12.29
ATOM	5794	CG	ARG	1284	43.569	19.576	8.085	1.00	16.09
ATOM	5795	CD	ARG	1284	42.703	18.923	9.135	1.00	20.20
ATOM	5796	NE	ARG	1284	41.326	18.588	8.722	1.00	21.27
ATOM	5797	CZ	ARG	1284	40.964	17.444	8.139	1.00	10.43
ATOM	5798	NH1	ARG	1284	41.871	16.526	7.861	1.00	16.46
ATOM	5799	NH2	ARG	1284	39.676	17.160	7.958	1.00	9.96
ATOM	5800	C	ARG	1284	47.268	20.678	8.327	1.00	17.27
ATOM	5801	O	ARG	1284	48.242	19.978	8.112	1.00	21.46
ATOM	5802	N	MET	1285	47.290	21.750	9.108	1.00	19.19
ATOM	5803	CA	MET	1285	48.455	22.173	9.878	1.00	19.83
ATOM	5804	CB	MET	1285	48.135	23.511	10.579	1.00	18.32
ATOM	5805	CG	MET	1285	49.320	24.226	11.260	1.00	21.37
ATOM	5806	SD	MET	1285	48.808	25.697	12.236	1.00	18.33
ATOM	5807	CE	MET	1285	50.344	26.231	12.870	1.00	15.58
ATOM	5808	C	MET	1285	48.713	21.115	10.935	1.00	19.93
ATOM	5809	O	MET	1285	47.775	20.540	11.477	1.00	16.24

Figure 23.42

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ATOM	5810	N	TRP	1286	49.974	20.897	11.272	1.00	19.54
ATOM	5811	CA	TRP	1286	50.304	19.919	12.296	1.00	18.41
ATOM	5812	CB	TRP	1286	51.751	19.501	12.137	1.00	18.01
ATOM	5813	CG	TRP	1286	52.088	18.229	12.802	1.00	20.70
ATOM	5814	CD2	TRP	1286	53.376	17.622	12.842	1.00	18.84
ATOM	5815	CE2	TRP	1286	53.266	16.443	13.612	1.00	20.91
ATOM	5816	CE3	TRP	1286	54.620	17.969	12.309	1.00	21.23
ATOM	5817	CD1	TRP	1286	51.253	17.411	13.519	1.00	18.64
ATOM	5818	NE1	TRP	1286	51.958	16.335	14.012	1.00	19.87
ATOM	5819	CZ2	TRP	1286	54.355	15.608	13.864	1.00	19.80
ATOM	5820	CZ3	TRP	1286	55.704	17.140	12.556	1.00	22.59
ATOM	5821	CH2	TRP	1286	55.564	15.971	13.328	1.00	16.66
ATOM	5822	C	TRP	1286	50.060	20.480	13.712	1.00	14.95
ATOM	5823	O	TRP	1286	50.987	20.798	14.436	1.00	15.10
ATOM	5824	N	HIS	1287	48.804	20.624	14.098	1.00	15.33
ATOM	5825	CA	HIS	1287	48.490	21.142	15.414	1.00	19.07
ATOM	5826	CB	HIS	1287	46.985	21.144	15.631	1.00	23.63
ATOM	5827	CG	HIS	1287	46.268	22.191	14.836	1.00	34.57
ATOM	5828	CD2	HIS	1287	45.328	22.091	13.864	1.00	35.23
ATOM	5829	ND1	HIS	1287	46.497	23.538	15.009	1.00	41.86
ATOM	5830	CE1	HIS	1287	45.731	24.225	14.181	1.00	43.57
ATOM	5831	NE2	HIS	1287	45.011	23.373	13.474	1.00	40.64
ATOM	5832	C	HIS	1287	49.167	20.309	16.486	1.00	19.76
ATOM	5833	O	HIS	1287	49.543	20.821	17.543	1.00	20.50
ATOM	5834	N	GLN	1288	49.377	19.038	16.178	1.00	21.58
ATOM	5835	CA	GLN	1288	50.009	18.107	17.105	1.00	25.74
ATOM	5836	CB	GLN	1288	49.775	16.676	16.633	1.00	27.82
ATOM	5837	CG	GLN	1288	48.325	16.204	16.796	1.00	34.64
ATOM	5838	CD	GLN	1288	47.846	16.193	18.252	1.00	39.87
ATOM	5839	OE1	GLN	1288	48.655	16.199	19.191	1.00	43.32
ATOM	5840	NE2	GLN	1288	46.525	16.183	18.444	1.00	40.01
ATOM	5841	C	GLN	1288	51.486	18.330	17.444	1.00	22.73
ATOM	5842	O	GLN	1288	51.970	17.815	18.456	1.00	30.74
ATOM	5881	N	GLY	1294	57.449	24.162	21.880	1.00	18.00
ATOM	5882	CA	GLY	1294	57.755	25.015	23.003	1.00	20.64
ATOM	5883	C	GLY	1294	57.397	26.468	22.759	1.00	21.76
ATOM	5884	O	GLY	1294	57.763	27.334	23.533	1.00	26.39
ATOM	5885	N	ASP	1295	56.725	26.763	21.662	1.00	21.95
ATOM	5886	CA	ASP	1295	56.340	28.140	21.397	1.00	17.91
ATOM	5887	CB	ASP	1295	56.141	28.370	19.893	1.00	19.96
ATOM	5888	CG	ASP	1295	57.432	28.231	19.101	1.00	15.94
ATOM	5889	OD1	ASP	1295	58.516	28.560	19.635	1.00	20.10
ATOM	5890	OD2	ASP	1295	57.351	27.806	17.925	1.00	16.30
ATOM	5891	C	ASP	1295	55.024	28.318	22.131	1.00	16.27
ATOM	5892	O	ASP	1295	54.368	27.329	22.447	1.00	14.67
ATOM	5893	N	LYS	1296	54.688	29.559	22.477	1.00	17.87
ATOM	5894	CA	LYS	1296	53.430	29.813	23.158	1.00	16.64
ATOM	5895	CB	LYS	1296	53.398	31.198	23.776	1.00	26.01
ATOM	5896	CG	LYS	1296	54.282	31.364	24.980	1.00	34.95
ATOM	5897	CD	LYS	1296	54.176	32.788	25.508	1.00	44.36
ATOM	5898	CE	LYS	1296	55.558	33.376	25.784	1.00	49.30
ATOM	5899	NZ	LYS	1296	55.429	34.748	26.355	1.00	54.50
ATOM	5900	C	LYS	1296	52.360	29.724	22.101	1.00	16.29
ATOM	5901	O	LYS	1296	52.506	30.290	21.033	1.00	19.55
ATOM	5902	N	VAL	1297	51.277	29.031	22.422	1.00	19.34
ATOM	5903	CA	VAL	1297	50.165	28.810	21.510	1.00	15.33
ATOM	5904	CB	VAL	1297	49.976	27.286	21.215	1.00	13.90
ATOM	5905	CG1	VAL	1297	48.886	27.074	20.194	1.00	14.41
ATOM	5906	CG2	VAL	1297	51.248	26.667	20.747	1.00	10.04

Figure 23.43

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ATOM	5907	C	VAL	1297	48.893	29.220	22.205	1.00	16.04
ATOM	5908	O	VAL	1297	48.723	28.923	23.393	1.00	19.62
ATOM	5909	N	ARG	1298	47.992	29.884	21.488	1.00	13.63
ATOM	5910	CA	ARG	1298	46.702	30.226	22.058	1.00	12.09
ATOM	5911	CB	ARG	1298	46.644	31.682	22.542	1.00	13.21
ATOM	5912	CG	ARG	1298	45.383	32.000	23.375	1.00	12.25
ATOM	5913	CD	ARG	1298	45.290	33.470	23.767	1.00	11.33
ATOM	5914	NE	ARG	1298	45.056	34.375	22.638	1.00	14.42
ATOM	5915	CZ	ARG	1298	45.973	35.176	22.102	1.00	13.34
ATOM	5916	NH1	ARG	1298	47.211	35.197	22.572	1.00	16.58
ATOM	5917	NH2	ARG	1298	45.647	35.971	21.090	1.00	12.19
ATOM	5918	C	ARG	1298	45.653	30.000	20.983	1.00	12.37
ATOM	5919	O	ARG	1298	45.919	30.200	19.806	1.00	15.30
ATOM	5920	N	MET	1299	44.489	29.506	21.366	1.00	12.41
ATOM	5921	CA	MET	1299	43.424	29.337	20.399	1.00	10.79
ATOM	5922	CB	MET	1299	42.731	27.980	20.524	1.00	13.84
ATOM	5923	CG	MET	1299	41.467	27.880	19.674	1.00	17.13
ATOM	5924	SD	MET	1299	40.885	26.225	19.406	1.00	19.68
ATOM	5925	CE	MET	1299	42.161	25.698	18.296	1.00	12.26
ATOM	5926	C	MET	1299	42.410	30.465	20.628	1.00	13.87
ATOM	5927	O	MET	1299	41.961	30.672	21.763	1.00	8.96
ATOM	5928	N	ASP	1300	42.058	31.175	19.555	1.00	13.31
ATOM	5929	CA	ASP	1300	41.093	32.264	19.610	1.00	9.27
ATOM	5930	CB	ASP	1300	41.693	33.558	19.066	1.00	14.09
ATOM	5931	CG	ASP	1300	42.500	34.328	20.094	1.00	14.70
ATOM	5932	OD1	ASP	1300	42.633	33.857	21.247	1.00	16.06
ATOM	5933	OD2	ASP	1300	43.009	35.408	19.737	1.00	20.44
ATOM	5934	C	ASP	1300	40.004	31.869	18.664	1.00	9.11
ATOM	5935	O	ASP	1300	40.231	31.083	17.760	1.00	11.34
ATOM	5936	N	PRO	1301	38.785	32.351	18.893	1.00	8.10
ATOM	5937	CD	PRO	1301	38.272	33.182	20.009	1.00	7.47
ATOM	5938	CA	PRO	1301	37.722	31.986	17.952	1.00	9.45
ATOM	5939	CB	PRO	1301	36.466	32.613	18.576	1.00	10.94
ATOM	5940	CG	PRO	1301	36.843	32.747	20.087	1.00	6.66
ATOM	5941	C	PRO	1301	38.155	32.711	16.645	1.00	10.72
ATOM	5942	O	PRO	1301	38.889	33.706	16.710	1.00	10.77
ATOM	5943	N	PRO	1302	37.772	32.197	15.456	1.00	7.99
ATOM	5944	CD	PRO	1302	36.830	31.085	15.219	1.00	7.42
ATOM	5945	CA	PRO	1302	38.139	32.812	14.183	1.00	9.36
ATOM	5946	CB	PRO	1302	37.499	31.878	13.176	1.00	9.92
ATOM	5947	CG	PRO	1302	36.256	31.446	13.890	1.00	6.38
ATOM	5948	C	PRO	1302	37.643	34.239	13.992	1.00	9.95
ATOM	5949	O	PRO	1302	36.445	34.499	14.117	1.00	13.82
ATOM	5950	N	CYS	1303	38.572	35.135	13.632	1.00	10.17
ATOM	5951	CA	CYS	1303	38.294	36.560	13.377	1.00	12.34
ATOM	5952	C	CYS	1303	37.784	37.291	14.580	1.00	11.83
ATOM	5953	O	CYS	1303	37.115	38.310	14.441	1.00	13.71
ATOM	5954	CB	CYS	1303	37.300	36.755	12.230	1.00	13.09
ATOM	5955	SG	CYS	1303	37.950	36.288	10.602	1.00	13.66
ATOM	5956	N	THR	1304	38.157	36.805	15.753	1.00	17.57
ATOM	5957	CA	THR	1304	37.708	37.374	17.005	1.00	18.74
ATOM	5958	CB	THR	1304	37.017	36.290	17.837	1.00	17.56
ATOM	5959	OG1	THR	1304	35.804	35.898	17.191	1.00	23.25
ATOM	5960	CG2	THR	1304	36.732	36.772	19.249	1.00	23.07
ATOM	5961	C	THR	1304	38.861	37.927	17.815	1.00	19.28
ATOM	5962	O	THR	1304	39.858	37.235	18.047	1.00	22.66
ATOM	5963	N	ASN	1305	38.692	39.168	18.266	1.00	22.15
ATOM	5964	CA	ASN	1305	39.685	39.859	19.086	1.00	24.22
ATOM	5965	CB	ASN	1305	39.723	41.336	18.729	1.00	27.21
ATOM	5966	CG	ASN	1305	40.682	42.119	19.595	1.00	24.55

Figure 23.44

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ATOM	5967	OD1	ASN	1305	41.494	41.564	20.318	1.00	22.42
ATOM	5968	ND2	ASN	1305	40.569	43.441	19.484	1.00	28.27
ATOM	5969	C	ASN	1305	39.251	39.670	20.542	1.00	24.27
ATOM	5970	O	ASN	1305	38.320	40.315	21.025	1.00	26.32
ATOM	5971	N	THR	1306	39.936	38.763	21.228	1.00	22.99
ATOM	5972	CA	THR	1306	39.639	38.432	22.609	1.00	20.50
ATOM	5973	CB	THR	1306	40.133	37.008	22.905	1.00	15.82
ATOM	5974	OG1	THR	1306	41.505	36.902	22.529	1.00	17.57
ATOM	5975	CG2	THR	1306	39.344	36.005	22.102	1.00	17.16
ATOM	5976	C	THR	1306	40.214	39.387	23.651	1.00	17.53
ATOM	5977	O	THR	1306	39.942	39.223	24.842	1.00	15.35
ATOM	5978	N	THR	1307	40.958	40.396	23.201	1.00	14.79
ATOM	5979	CA	THR	1307	41.599	41.363	24.090	1.00	19.15
ATOM	5980	CB	THR	1307	42.352	42.433	23.298	1.00	21.40
ATOM	5981	OG1	THR	1307	43.348	41.795	22.489	1.00	26.67
ATOM	5982	CG2	THR	1307	43.048	43.422	24.247	1.00	25.86
ATOM	5983	C	THR	1307	40.735	42.039	25.157	1.00	16.30
ATOM	5984	O	THR	1307	41.047	41.948	26.333	1.00	17.06
ATOM	5985	N	ALA	1308	39.696	42.755	24.760	1.00	15.01
ATOM	5986	CA	ALA	1308	38.834	43.404	25.722	1.00	14.41
ATOM	5987	CB	ALA	1308	37.578	43.908	25.028	1.00	14.08
ATOM	5988	C	ALA	1308	38.471	42.454	26.885	1.00	18.25
ATOM	5989	O	ALA	1308	38.829	42.715	28.033	1.00	21.28
ATOM	5990	N	ALA	1309	37.823	41.331	26.569	1.00	17.96
ATOM	5991	CA	ALA	1309	37.411	40.331	27.560	1.00	14.58
ATOM	5992	CB	ALA	1309	36.617	39.239	26.895	1.00	10.46
ATOM	5993	C	ALA	1309	38.546	39.724	28.393	1.00	15.70
ATOM	5994	O	ALA	1309	38.443	39.633	29.617	1.00	17.76
ATOM	5995	N	SER	1310	39.631	39.336	27.745	1.00	10.89
ATOM	5996	CA	SER	1310	40.756	38.751	28.431	1.00	11.22
ATOM	5997	CB	SER	1310	41.742	38.236	27.420	1.00	6.17
ATOM	5998	OG	SER	1310	42.884	37.677	28.040	1.00	14.61
ATOM	5999	C	SER	1310	41.414	39.768	29.328	1.00	20.38
ATOM	6000	O	SER	1310	41.874	39.437	30.427	1.00	21.24
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ATOM	6131	N	GLN	1327	45.603	30.761	42.510	1.00	24.88
ATOM	6132	CA	GLN	1327	46.475	29.782	41.879	1.00	26.79
ATOM	6133	CB	GLN	1327	46.504	28.485	42.705	1.00	31.85
ATOM	6134	CG	GLN	1327	45.367	27.496	42.400	1.00	37.11
ATOM	6135	CD	GLN	1327	44.321	27.415	43.501	1.00	45.27
ATOM	6136	OE1	GLN	1327	44.203	28.338	44.325	1.00	51.95
ATOM	6137	NE2	GLN	1327	43.534	26.318	43.508	1.00	41.15
ATOM	6138	C	GLN	1327	46.093	29.478	40.422	1.00	24.68
ATOM	6139	O	GLN	1327	46.959	29.135	39.622	1.00	27.37
ATOM	6140	N	LEU	1328	44.808	29.566	40.085	1.00	20.03
ATOM	6141	CA	LEU	1328	44.366	29.289	38.724	1.00	16.82
ATOM	6142	CB	LEU	1328	42.876	29.581	38.577	1.00	14.85
ATOM	6143	CG	LEU	1328	41.969	28.731	39.456	1.00	17.98
ATOM	6144	CD1	LEU	1328	40.534	29.008	39.110	1.00	14.73
ATOM	6145	CD2	LEU	1328	42.280	27.256	39.267	1.00	19.60
ATOM	6146	C	LEU	1328	45.159	30.122	37.723	1.00	17.22
ATOM	6147	O	LEU	1328	45.492	31.278	38.004	1.00	18.76
ATOM	6148	N	PRO	1329	45.531	29.532	36.562	1.00	16.86
ATOM	6149	CD	PRO	1329	45.201	28.176	36.074	1.00	17.84
ATOM	6150	CA	PRO	1329	46.296	30.268	35.547	1.00	15.49
ATOM	6151	CB	PRO	1329	46.741	29.165	34.599	1.00	17.24
ATOM	6152	CG	PRO	1329	45.570	28.247	34.616	1.00	13.96
ATOM	6153	C	PRO	1329	45.391	31.276	34.854	1.00	17.40
ATOM	6154	O	PRO	1329	44.161	31.281	35.074	1.00	18.71
ATOM	6155	N	GLN	1330	45.997	32.122	34.021	1.00	21.18

Figure 23.45

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ATOM	6156	CA	GLN	1330	45.253	33.162	33.319	1.00	22.07
ATOM	6157	CB	GLN	1330	46.171	34.056	32.499	1.00	24.05
ATOM	6158	CG	GLN	1330	46.602	33.452	31.198	1.00	35.03
ATOM	6159	CD	GLN	1330	47.345	34.440	30.341	1.00	36.38
ATOM	6160	OE1	GLN	1330	46.902	34.768	29.247	1.00	37.43
ATOM	6161	NE2	GLN	1330	48.493	34.912	30.827	1.00	41.64
ATOM	6162	C	GLN	1330	44.137	32.663	32.444	1.00	20.80
ATOM	6163	O	GLN	1330	44.210	31.580	31.864	1.00	20.17
ATOM	6164	N	TRP	1331	43.114	33.500	32.355	1.00	19.19
ATOM	6165	CA	TRP	1331	41.917	33.259	31.582	1.00	15.74
ATOM	6166	CB	TRP	1331	40.811	34.209	32.086	1.00	9.68
ATOM	6167	CG	TRP	1331	39.433	33.939	31.543	1.00	7.90
ATOM	6168	CD2	TRP	1331	38.861	34.476	30.337	1.00	9.80
ATOM	6169	CE2	TRP	1331	37.568	33.927	30.207	1.00	10.42
ATOM	6170	CE3	TRP	1331	39.322	35.370	29.346	1.00	12.32
ATOM	6171	CD1	TRP	1331	38.490	33.117	32.079	1.00	8.51
ATOM	6172	NE1	TRP	1331	37.366	33.107	31.290	1.00	5.81
ATOM	6173	CZ2	TRP	1331	36.713	34.239	29.124	1.00	11.58
ATOM	6174	CZ3	TRP	1331	38.474	35.681	28.265	1.00	4.60
ATOM	6175	CH2	TRP	1331	37.185	35.114	28.171	1.00	7.15
ATOM	6176	C	TRP	1331	42.179	33.537	30.100	1.00	17.56
ATOM	6177	O	TRP	1331	42.880	34.495	29.752	1.00	16.46
ATOM	6178	N	ASP	1332	41.675	32.644	29.248	1.00	17.58
ATOM	6179	CA	ASP	1332	41.743	32.767	27.791	1.00	15.86
ATOM	6180	CB	ASP	1332	42.677	31.745	27.134	1.00	15.21
ATOM	6181	CG	ASP	1332	44.105	31.867	27.590	1.00	14.99
ATOM	6182	OD1	ASP	1332	44.740	32.912	27.336	1.00	17.52
ATOM	6183	OD2	ASP	1332	44.607	30.878	28.182	1.00	24.22
ATOM	6184	C	ASP	1332	40.323	32.399	27.419	1.00	13.51
ATOM	6185	O	ASP	1332	39.692	31.615	28.142	1.00	13.41
ATOM	6186	N	MET	1333	39.813	32.955	26.319	1.00	13.87
ATOM	6187	CA	MET	1333	38.451	32.644	25.885	1.00	11.98
ATOM	6188	CB	MET	1333	37.995	33.568	24.754	1.00	14.30
ATOM	6189	CG	MET	1333	36.467	33.720	24.669	1.00	15.28
ATOM	6190	SD	MET	1333	36.010	34.950	23.447	1.00	32.07
ATOM	6191	CE	MET	1333	36.098	36.463	24.442	1.00	17.03
ATOM	6192	C	MET	1333	38.296	31.179	25.477	1.00	7.62
ATOM	6193	O	MET	1333	37.257	30.557	25.735	1.00	10.01
ATOM	6194	N	CYS	1334	39.347	30.607	24.903	1.00	10.15
ATOM	6195	CA	CYS	1334	39.318	29.205	24.494	1.00	12.87
ATOM	6196	C	CYS	1334	40.586	28.551	24.978	1.00	10.05
ATOM	6197	O	CYS	1334	41.649	29.202	25.012	1.00	11.91
ATOM	6198	CB	CYS	1334	39.277	29.041	22.948	1.00	12.65
ATOM	6199	SG	CYS	1334	37.837	29.735	22.072	1.00	13.22
ATOM	6200	N	ASN	1335	40.489	27.277	25.368	1.00	12.61
ATOM	6201	CA	ASN	1335	41.688	26.550	25.763	1.00	11.39
ATOM	6202	CB	ASN	1335	41.482	25.711	27.021	1.00	11.86
ATOM	6203	CG	ASN	1335	42.794	25.159	27.535	1.00	11.49
ATOM	6204	OD1	ASN	1335	43.336	24.212	26.981	1.00	21.62
ATOM	6205	ND2	ASN	1335	43.373	25.832	28.514	1.00	23.00
ATOM	6206	C	ASN	1335	42.165	25.646	24.606	1.00	8.19
ATOM	6207	O	ASN	1335	41.466	24.711	24.199	1.00	9.72
ATOM	6208	N	PHE	1336	43.339	25.948	24.065	1.00	11.32
ATOM	6209	CA	PHE	1336	43.903	25.174	22.968	1.00	13.29
ATOM	6210	CB	PHE	1336	45.292	25.693	22.614	1.00	11.35
ATOM	6211	CG	PHE	1336	46.031	24.822	21.627	1.00	20.08
ATOM	6212	CD1	PHE	1336	45.544	24.630	20.332	1.00	18.83
ATOM	6213	CD2	PHE	1336	47.227	24.190	21.993	1.00	15.81
ATOM	6214	CE1	PHE	1336	46.241	23.820	19.418	1.00	18.03
ATOM	6215	CE2	PHE	1336	47.924	23.381	21.087	1.00	18.32

Figure 23.46

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ATOM	6216	CZ	PHE	1336	47.432	23.198	19.802	1.00	15.81
ATOM	6217	C	PHE	1336	43.959	23.682	23.289	1.00	13.67
ATOM	6218	O	PHE	1336	43.398	22.872	22.569	1.00	15.69
ATOM	6219	N	LEU	1337	44.643	23.328	24.371	1.00	16.29
ATOM	6220	CA	LEU	1337	44.772	21.939	24.786	1.00	14.49
ATOM	6221	CB	LEU	1337	45.577	21.864	26.066	1.00	18.32
ATOM	6222	CG	LEU	1337	46.992	21.442	25.697	1.00	24.74
ATOM	6223	CD1	LEU	1337	48.008	22.158	26.525	1.00	29.97
ATOM	6224	CD2	LEU	1337	47.123	19.932	25.829	1.00	27.19
ATOM	6225	C	LEU	1337	43.464	21.187	24.937	1.00	14.74
ATOM	6226	O	LEU	1337	43.357	20.025	24.525	1.00	16.63
ATOM	6227	N	VAL	1338	42.461	21.839	25.517	1.00	10.36
ATOM	6228	CA	VAL	1338	41.158	21.206	25.676	1.00	10.04
ATOM	6229	CB	VAL	1338	40.137	22.110	26.402	1.00	8.16
ATOM	6230	CG1	VAL	1338	38.744	21.478	26.320	1.00	10.40
ATOM	6231	CG2	VAL	1338	40.523	22.294	27.868	1.00	12.50
ATOM	6232	C	VAL	1338	40.582	20.852	24.308	1.00	14.79
ATOM	6233	O	VAL	1338	40.089	19.745	24.102	1.00	15.49
ATOM	6234	N	ASN	1339	40.612	21.823	23.394	1.00	18.63
ATOM	6235	CA	ASN	1339	40.106	21.672	22.015	1.00	18.12
ATOM	6236	CB	ASN	1339	40.218	23.019	21.282	1.00	8.67
ATOM	6237	CG	ASN	1339	39.718	22.950	19.866	1.00	5.10
ATOM	6238	OD1	ASN	1339	40.490	22.743	18.946	1.00	8.82
ATOM	6239	ND2	ASN	1339	38.430	23.146	19.680	1.00	5.01
ATOM	6240	C	ASN	1339	40.875	20.581	21.247	1.00	14.35
ATOM	6241	O	ASN	1339	40.279	19.655	20.682	1.00	10.62
ATOM	6242	N	LEU	1340	42.199	20.685	21.285	1.00	13.18
ATOM	6243	CA	LEU	1340	43.110	19.745	20.646	1.00	16.72
ATOM	6244	CB	LEU	1340	44.563	20.126	20.961	1.00	13.44
ATOM	6245	CG	LEU	1340	45.659	19.179	20.460	1.00	12.01
ATOM	6246	CD1	LEU	1340	45.978	19.476	18.998	1.00	15.80
ATOM	6247	CD2	LEU	1340	46.917	19.367	21.274	1.00	15.88
ATOM	6248	C	LEU	1340	42.902	18.303	21.105	1.00	18.71
ATOM	6249	O	LEU	1340	42.970	17.374	20.301	1.00	18.27
ATOM	6250	N	GLN	1341	42.699	18.106	22.403	1.00	17.49
ATOM	6251	CA	GLN	1341	42.541	16.761	22.939	1.00	12.85
ATOM	6252	CB	GLN	1341	43.155	16.651	24.325	1.00	15.30
ATOM	6253	CG	GLN	1341	44.524	17.268	24.488	1.00	19.46
ATOM	6254	CD	GLN	1341	45.016	17.144	25.916	1.00	25.14
ATOM	6255	OE1	GLN	1341	44.551	17.844	26.827	1.00	25.07
ATOM	6256	NE2	GLN	1341	45.927	16.210	26.131	1.00	31.90
ATOM	6257	C	GLN	1341	41.110	16.307	23.032	1.00	14.53
ATOM	6258	O	GLN	1341	40.854	15.199	23.495	1.00	17.43
ATOM	6259	N	TYR	1342	40.171	17.146	22.624	1.00	9.28
ATOM	6260	CA	TYR	1342	38.778	16.771	22.700	1.00	10.17
ATOM	6261	CB	TYR	1342	37.897	17.952	22.384	1.00	6.11
ATOM	6262	CG	TYR	1342	36.485	17.736	22.814	1.00	2.40
ATOM	6263	CD1	TYR	1342	36.093	18.006	24.127	1.00	4.27
ATOM	6264	CE1	TYR	1342	34.761	17.852	24.531	1.00	4.78
ATOM	6265	CD2	TYR	1342	35.533	17.302	21.921	1.00	2.00
ATOM	6266	CE2	TYR	1342	34.200	17.136	22.312	1.00	3.49
ATOM	6267	CZ	TYR	1342	33.819	17.413	23.611	1.00	2.00
ATOM	6268	OH	TYR	1342	32.504	17.277	23.984	1.00	5.33
ATOM	6269	C	TYR	1342	38.416	15.643	21.766	1.00	13.26
ATOM	6270	O	TYR	1342	38.923	15.579	20.640	1.00	16.99
ATOM	6271	N	ARG	1343	37.515	14.769	22.212	1.00	14.41
ATOM	6272	CA	ARG	1343	37.065	13.677	21.377	1.00	13.13
ATOM	6273	CB	ARG	1343	37.434	12.310	21.974	1.00	21.72
ATOM	6274	CG	ARG	1343	37.145	11.155	21.023	1.00	29.33
ATOM	6275	CD	ARG	1343	37.482	9.801	21.614	1.00	36.24

Figure 23.47

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ATOM	6276	NE	ARG	1343	37.233	8.708	20.665	1.00	41.97
ATOM	6277	CZ	ARG	1343	36.967	7.451	21.016	1.00	43.51
ATOM	6278	NH1	ARG	1343	36.894	7.112	22.293	1.00	43.48
ATOM	6279	NH2	ARG	1343	36.842	6.509	20.093	1.00	46.91
ATOM	6280	C	ARG	1343	35.579	13.754	21.111	1.00	9.94
ATOM	6281	O	ARG	1343	34.777	13.597	22.024	1.00	11.17
ATOM	6282	N	ARG	1344	35.234	14.079	19.867	1.00	8.12
ATOM	6283	CA	ARG	1344	33.849	14.145	19.414	1.00	8.61
ATOM	6284	CB	ARG	1344	33.734	14.886	18.063	1.00	14.65
ATOM	6285	CG	ARG	1344	33.857	16.406	18.131	1.00	10.51
ATOM	6286	CD	ARG	1344	34.659	16.944	16.960	1.00	8.72
ATOM	6287	NE	ARG	1344	35.026	18.335	17.134	1.00	2.00
ATOM	6288	CZ	ARG	1344	36.239	18.747	17.466	1.00	3.84
ATOM	6289	NH1	ARG	1344	37.195	17.850	17.663	1.00	3.04
ATOM	6290	NH2	ARG	1344	36.507	20.057	17.581	1.00	8.47
ATOM	6291	C	ARG	1344	33.444	12.687	19.236	1.00	11.40
ATOM	6292	O	ARG	1344	34.195	11.895	18.671	1.00	15.60
ATOM	6293	N	LEU	1345	32.251	12.343	19.704	1.00	12.92
ATOM	6294	CA	LEU	1345	31.776	10.973	19.650	1.00	13.42
ATOM	6295	CB	LEU	1345	31.587	10.441	21.086	1.00	12.78
ATOM	6296	CG	LEU	1345	32.757	10.503	22.086	1.00	9.34
ATOM	6297	CD1	LEU	1345	32.279	10.006	23.449	1.00	11.82
ATOM	6298	CD2	LEU	1345	33.948	9.691	21.611	1.00	9.90
ATOM	6299	C	LEU	1345	30.479	10.789	18.867	1.00	13.74
ATOM	6300	O	LEU	1345	30.296	9.776	18.200	1.00	14.74
ATOM	6301	N	TYR	1346	29.545	11.721	19.016	1.00	13.44
ATOM	6302	CA	TYR	1346	28.268	11.627	18.317	1.00	15.12
ATOM	6303	CB	TYR	1346	27.211	12.475	18.991	1.00	12.59
ATOM	6304	CG	TYR	1346	26.861	11.962	20.353	1.00	16.63
ATOM	6305	CD1	TYR	1346	27.387	12.551	21.500	1.00	15.96
ATOM	6306	CE1	TYR	1346	27.068	12.085	22.748	1.00	19.57
ATOM	6307	CD2	TYR	1346	26.010	10.883	20.496	1.00	19.19
ATOM	6308	CE2	TYR	1346	25.685	10.400	21.740	1.00	21.89
ATOM	6309	CZ	TYR	1346	26.214	11.006	22.870	1.00	22.13
ATOM	6310	OH	TYR	1346	25.859	10.544	24.116	1.00	25.59
ATOM	6311	C	TYR	1346	28.443	12.094	16.903	1.00	16.81
ATOM	6312	O	TYR	1346	29.268	12.957	16.631	1.00	21.14
ATOM	6313	N	ARG	1347	27.665	11.515	16.003	1.00	19.07
ATOM	6314	CA	ARG	1347	27.738	11.864	14.594	1.00	20.79
ATOM	6315	CB	ARG	1347	27.398	10.618	13.762	1.00	27.99
ATOM	6316	CG	ARG	1347	27.725	10.703	12.274	1.00	39.49
ATOM	6317	CD	ARG	1347	27.515	9.351	11.578	1.00	49.20
ATOM	6318	NE	ARG	1347	26.312	9.312	10.744	1.00	60.26
ATOM	6319	CZ	ARG	1347	25.070	9.200	11.216	1.00	68.75
ATOM	6320	NH1	ARG	1347	24.857	9.109	12.524	1.00	70.26
ATOM	6321	NH2	ARG	1347	24.031	9.202	10.383	1.00	74.59
ATOM	6322	C	ARG	1347	26.759	13.003	14.299	1.00	15.82
ATOM	6323	O	ARG	1347	27.036	13.865	13.471	1.00	16.50
ATOM	6324	N	SER	1348	25.653	13.011	15.042	1.00	15.40
ATOM	6325	CA	SER	1348	24.576	13.974	14.901	1.00	14.60
ATOM	6326	CB	SER	1348	23.741	13.638	13.634	1.00	14.11
ATOM	6327	OG	SER	1348	22.346	13.446	13.884	1.00	20.31
ATOM	6328	C	SER	1348	23.697	13.916	16.152	1.00	14.62
ATOM	6329	O	SER	1348	23.724	12.924	16.886	1.00	18.91
ATOM	6330	N	MET	1349	22.894	14.959	16.352	1.00	13.16
ATOM	6331	CA	MET	1349	21.990	15.092	17.496	1.00	13.39
ATOM	6332	CB	MET	1349	21.921	16.565	17.926	1.00	12.12
ATOM	6333	CG	MET	1349	23.222	17.083	18.548	1.00	9.38
ATOM	6334	SD	MET	1349	23.674	16.189	20.099	1.00	11.99
ATOM	6335	CE	MET	1349	25.015	15.158	19.578	1.00	7.72

Figure 23.48

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ATOM	6336	C	MET	1349	20.581	14.577	17.239	1.00	12.37
ATOM	6337	O	MET	1349	19.670	14.796	18.058	1.00	13.03
ATOM	6338	N	ASN	1350	20.406	13.884	16.113	1.00	14.56
ATOM	6339	CA	ASN	1350	19.101	13.357	15.728	1.00	15.80
ATOM	6340	CB	ASN	1350	19.226	12.585	14.398	1.00	20.93
ATOM	6341	CG	ASN	1350	17.921	11.893	13.982	1.00	21.97
ATOM	6342	OD1	ASN	1350	17.728	10.709	14.274	1.00	25.95
ATOM	6343	ND2	ASN	1350	17.033	12.615	13.286	1.00	23.78
ATOM	6344	C	ASN	1350	18.439	12.511	16.827	1.00	16.55
ATOM	6345	O	ASN	1350	17.305	12.798	17.254	1.00	17.81
ATOM	6481	N	TYR	1367	17.962	28.227	16.494	1.00	6.02
ATOM	6482	CA	TYR	1367	17.931	29.500	15.804	1.00	5.74
ATOM	6483	CB	TYR	1367	17.436	30.624	16.737	1.00	10.60
ATOM	6484	CG	TYR	1367	18.328	30.911	17.917	1.00	10.03
ATOM	6485	CD1	TYR	1367	19.341	31.849	17.811	1.00	8.60
ATOM	6486	CE1	TYR	1367	20.232	32.054	18.823	1.00	10.34
ATOM	6487	CD2	TYR	1367	18.221	30.182	19.108	1.00	7.91
ATOM	6488	CE2	TYR	1367	19.128	30.382	20.143	1.00	6.03
ATOM	6489	CZ	TYR	1367	20.132	31.318	19.980	1.00	12.63
ATOM	6490	OH	TYR	1367	21.098	31.510	20.921	1.00	16.15
ATOM	6491	C	TYR	1367	19.292	29.774	15.204	1.00	6.67
ATOM	6492	O	TYR	1367	20.311	29.466	15.812	1.00	6.01
ATOM	6493	N	ASN	1368	19.309	30.270	13.976	1.00	10.44
ATOM	6494	CA	ASN	1368	20.576	30.519	13.293	1.00	7.58
ATOM	6495	CB	ASN	1368	20.793	29.503	12.151	1.00	3.77
ATOM	6496	CG	ASN	1368	21.153	28.108	12.640	1.00	4.12
ATOM	6497	OD1	ASN	1368	20.332	27.411	13.221	1.00	7.87
ATOM	6498	ND2	ASN	1368	22.363	27.668	12.328	1.00	3.22
ATOM	6499	C	ASN	1368	20.640	31.893	12.649	1.00	4.00
ATOM	6500	O	ASN	1368	19.684	32.329	12.027	1.00	11.97
ATOM	6501	N	GLY	1369	21.767	32.568	12.823	1.00	8.85
ATOM	6502	CA	GLY	1369	21.981	33.839	12.172	1.00	8.13
ATOM	6503	C	GLY	1369	22.323	33.430	10.751	1.00	7.52
ATOM	6504	O	GLY	1369	23.222	32.604	10.548	1.00	7.14
ATOM	6505	N	ASP	1370	21.615	33.989	9.775	1.00	12.01
ATOM	6506	CA	ASP	1370	21.809	33.609	8.370	1.00	10.99
ATOM	6507	CB	ASP	1370	20.514	33.855	7.603	1.00	8.82
ATOM	6508	CG	ASP	1370	20.165	35.330	7.489	1.00	7.50
ATOM	6509	OD1	ASP	1370	20.992	36.196	7.823	1.00	4.05
ATOM	6510	OD2	ASP	1370	19.057	35.624	7.018	1.00	5.18
ATOM	6511	C	ASP	1370	23.022	34.034	7.518	1.00	7.16
ATOM	6512	O	ASP	1370	23.037	33.741	6.316	1.00	9.67
ATOM	6513	N	VAL	1371	24.024	34.687	8.119	1.00	3.88
ATOM	6514	CA	VAL	1371	25.233	35.124	7.402	1.00	3.42
ATOM	6515	CB	VAL	1371	25.383	36.692	7.313	1.00	6.68
ATOM	6516	CG1	VAL	1371	24.090	37.309	6.845	1.00	5.56
ATOM	6517	CG2	VAL	1371	25.777	37.277	8.616	1.00	9.26
ATOM	6518	C	VAL	1371	26.483	34.489	8.001	1.00	3.95
ATOM	6519	O	VAL	1371	27.621	34.862	7.711	1.00	9.43
ATOM	6520	N	ASP	1372	26.236	33.509	8.853	1.00	4.54
ATOM	6521	CA	ASP	1372	27.281	32.743	9.500	1.00	7.15
ATOM	6522	CB	ASP	1372	26.713	32.129	10.782	1.00	5.20
ATOM	6523	CG	ASP	1372	27.638	31.126	11.410	1.00	2.00
ATOM	6524	OD1	ASP	1372	28.849	31.353	11.441	1.00	5.12
ATOM	6525	OD2	ASP	1372	27.129	30.089	11.879	1.00	9.13
ATOM	6526	C	ASP	1372	27.645	31.617	8.552	1.00	3.35
ATOM	6527	O	ASP	1372	26.777	31.086	7.858	1.00	8.14
ATOM	6528	N	MET	1373	28.918	31.234	8.573	1.00	4.20
ATOM	6529	CA	MET	1373	29.403	30.143	7.748	1.00	8.15

Figure 23.49

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ATOM	6530	CB	MET	1373	30.465	30.657	6.771	1.00	12.00
ATOM	6531	CG	MET	1373	29.968	31.747	5.838	1.00	8.48
ATOM	6532	SD	MET	1373	31.081	32.014	4.499	1.00	11.70
ATOM	6533	CE	MET	1373	32.365	32.981	5.268	1.00	2.75
ATOM	6534	C	MET	1373	29.968	28.970	8.595	1.00	11.20
ATOM	6535	O	MET	1373	30.229	27.884	8.059	1.00	12.21
ATOM	6536	N	ALA	1374	30.157	29.194	9.905	1.00	9.28
ATOM	6537	CA	ALA	1374	30.671	28.157	10.802	1.00	5.98
ATOM	6538	CB	ALA	1374	31.216	28.764	12.090	1.00	3.14
ATOM	6539	C	ALA	1374	29.581	27.134	11.090	1.00	2.00
ATOM	6540	O	ALA	1374	29.851	25.953	11.134	1.00	10.17
ATOM	6541	N	CYS	1375	28.341	27.587	11.253	1.00	3.77
ATOM	6542	CA	CYS	1375	27.184	26.700	11.478	1.00	5.23
ATOM	6543	CB	CYS	1375	26.853	26.503	12.980	1.00	8.90
ATOM	6544	SG	CYS	1375	27.943	25.434	14.011	1.00	11.46
ATOM	6545	C	CYS	1375	26.005	27.348	10.742	1.00	7.20
ATOM	6546	O	CYS	1375	24.981	27.718	11.349	1.00	8.32
ATOM	6547	N	ASN	1376	26.155	27.491	9.427	1.00	7.19
ATOM	6548	CA	ASN	1376	25.137	28.123	8.581	1.00	5.23
ATOM	6549	CB	ASN	1376	25.499	28.012	7.093	1.00	4.07
ATOM	6550	CG	ASN	1376	25.125	26.652	6.471	1.00	5.32
ATOM	6551	OD1	ASN	1376	23.975	26.432	6.108	1.00	6.48
ATOM	6552	ND2	ASN	1376	26.112	25.771	6.307	1.00	3.48
ATOM	6553	C	ASN	1376	23.715	27.649	8.852	1.00	7.03
ATOM	6554	O	ASN	1376	23.498	26.526	9.335	1.00	13.20
ATOM	6555	N	PHE	1377	22.758	28.557	8.652	1.00	9.98
ATOM	6556	CA	PHE	1377	21.356	28.276	8.888	1.00	7.71
ATOM	6557	CB	PHE	1377	20.517	29.524	8.587	1.00	7.80
ATOM	6558	CG	PHE	1377	20.270	29.745	7.098	1.00	9.44
ATOM	6559	CD1	PHE	1377	19.120	29.235	6.489	1.00	11.63
ATOM	6560	CD2	PHE	1377	21.236	30.354	6.287	1.00	5.43
ATOM	6561	CE1	PHE	1377	18.954	29.325	5.105	1.00	8.50
ATOM	6562	CE2	PHE	1377	21.059	30.438	4.906	1.00	2.70
ATOM	6563	CZ	PHE	1377	19.926	29.926	4.326	1.00	4.61
ATOM	6564	C	PHE	1377	20.782	27.095	8.076	1.00	11.99
ATOM	6565	O	PHE	1377	19.794	26.477	8.500	1.00	10.68
ATOM	6566	N	MET	1378	21.349	26.829	6.892	1.00	11.15
ATOM	6567	CA	MET	1378	20.817	25.778	6.019	1.00	13.98
ATOM	6568	CB	MET	1378	21.396	25.884	4.607	1.00	15.25
ATOM	6569	CG	MET	1378	20.775	24.872	3.654	1.00	17.89
ATOM	6570	SD	MET	1378	20.839	25.303	1.920	1.00	17.94
ATOM	6571	CE	MET	1378	19.396	26.394	1.807	1.00	2.03
ATOM	6572	C	MET	1378	21.026	24.390	6.580	1.00	10.20
ATOM	6573	O	MET	1378	20.097	23.583	6.589	1.00	16.11
ATOM	6574	N	GLY	1379	22.258	24.121	7.008	1.00	11.19
ATOM	6575	CA	GLY	1379	22.613	22.857	7.631	1.00	10.74
ATOM	6576	C	GLY	1379	21.704	22.588	8.817	1.00	11.28
ATOM	6577	O	GLY	1379	21.300	21.449	9.045	1.00	13.51
ATOM	6578	N	ASP	1380	21.358	23.631	9.566	1.00	8.03
ATOM	6579	CA	ASP	1380	20.472	23.448	10.695	1.00	8.63
ATOM	6580	CB	ASP	1380	20.692	24.475	11.794	1.00	11.80
ATOM	6581	CG	ASP	1380	21.752	24.031	12.784	1.00	10.38
ATOM	6582	OD1	ASP	1380	21.731	22.847	13.159	1.00	15.61
ATOM	6583	OD2	ASP	1380	22.613	24.842	13.171	1.00	9.23
ATOM	6584	C	ASP	1380	19.025	23.391	10.293	1.00	9.86
ATOM	6585	O	ASP	1380	18.205	22.786	11.002	1.00	14.03
ATOM	6586	N	GLU	1381	18.687	23.980	9.152	1.00	8.46
ATOM	6587	CA	GLU	1381	17.307	23.898	8.721	1.00	5.09
ATOM	6588	CB	GLU	1381	16.971	24.937	7.682	1.00	8.59
ATOM	6589	CG	GLU	1381	15.495	24.966	7.476	1.00	4.08

Figure 23.50

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ATOM    6590   CD   GLU   1381     15.018  26.242   6.827  1.00   4.49
ATOM    6591   OE1  GLU   1381     15.863  27.054   6.384  1.00  11.09
ATOM    6592   OE2  GLU   1381     13.781  26.417   6.768  1.00  11.03
ATOM    6593   C    GLU   1381     17.066  22.517   8.156  1.00   6.96
ATOM    6594   O    GLU   1381     15.987  21.954   8.319  1.00  12.20
===================================================================
ATOM    6937   N    THR   1423     15.464  31.718  11.756  1.00  10.99
ATOM    6938   CA   THR   1423     16.651  32.454  11.282  1.00  10.26
ATOM    6939   CB   THR   1423     16.798  32.528   9.688  1.00   7.48
ATOM    6940   OG1  THR   1423     15.685  33.225   9.116  1.00   9.08
ATOM    6941   CG2  THR   1423     16.921  31.150   9.042  1.00   8.47
ATOM    6942   C    THR   1423     16.612  33.910  11.793  1.00   9.78
ATOM    6943   O    THR   1423     15.547  34.470  12.073  1.00   5.61
ATOM    6944   N    ILE   1424     17.788  34.490  11.967  1.00   7.28
ATOM    6945   CA   ILE   1424     17.901  35.874  12.358  1.00   8.19
ATOM    6946   CB   ILE   1424     18.678  36.073  13.701  1.00   9.12
ATOM    6947   CG2  ILE   1424     18.729  37.541  14.043  1.00   6.85
ATOM    6948   CG1  ILE   1424     17.944  35.367  14.851  1.00   8.03
ATOM    6949   CD1  ILE   1424     18.228  33.863  14.983  1.00   5.48
ATOM    6950   C    ILE   1424     18.638  36.458  11.157  1.00   6.43
ATOM    6951   O    ILE   1424     19.788  36.099  10.854  1.00   8.58
ATOM    6952   N    LYS   1425     17.882  37.209  10.378  1.00   8.84
ATOM    6953   CA   LYS   1425     18.361  37.827   9.156  1.00   9.84
ATOM    6954   CB   LYS   1425     17.161  38.396   8.400  1.00  10.43
ATOM    6955   CG   LYS   1425     17.444  38.876   6.984  1.00   4.68
ATOM    6956   CD   LYS   1425     16.129  39.278   6.318  1.00   4.69
ATOM    6957   CE   LYS   1425     15.539  40.527   6.974  1.00   4.47
ATOM    6958   NZ   LYS   1425     16.337  41.769   6.682  1.00   2.00
ATOM    6959   C    LYS   1425     19.401  38.892   9.441  1.00   9.26
ATOM    6960   O    LYS   1425     19.142  39.805  10.192  1.00  10.59
ATOM    6961   N    GLY   1426     20.581  38.758   8.843  1.00   8.92
ATOM    6962   CA   GLY   1426     21.642  39.719   9.072  1.00   5.66
ATOM    6963   C    GLY   1426     22.575  39.389  10.226  1.00   6.86
ATOM    6964   O    GLY   1426     23.549  40.108  10.446  1.00   7.21
ATOM    6965   N    ALA   1427     22.297  38.300  10.952  1.00   7.01
ATOM    6966   CA   ALA   1427     23.114  37.877  12.094  1.00   5.23
ATOM    6967   CB   ALA   1427     22.208  37.415  13.248  1.00   4.59
ATOM    6968   C    ALA   1427     24.104  36.773  11.743  1.00   7.23
ATOM    6969   O    ALA   1427     23.833  35.937  10.880  1.00  11.45
ATOM    6970   N    GLY   1428     25.256  36.798  12.392  1.00   4.17
ATOM    6971   CA   GLY   1428     26.266  35.791  12.192  1.00   2.76
ATOM    6972   C    GLY   1428     26.173  34.717  13.267  1.00   5.55
ATOM    6973   O    GLY   1428     25.132  34.512  13.862  1.00   7.07
ATOM    6974   N    HIS   1429     27.299  34.087  13.565  1.00   8.47
ATOM    6975   CA   HIS   1429     27.393  33.001  14.537  1.00   9.30
ATOM    6976   CB   HIS   1429     28.834  32.509  14.572  1.00   7.05
ATOM    6977   CG   HIS   1429     28.976  31.073  14.968  1.00   8.37
ATOM    6978   CD2  HIS   1429     29.797  30.470  15.854  1.00   6.41
ATOM    6979   ND1  HIS   1429     28.242  30.067  14.384  1.00   8.28
ATOM    6980   CE1  HIS   1429     28.614  28.905  14.882  1.00  11.00
ATOM    6981   NE2  HIS   1429     29.555  29.124  15.777  1.00   4.85
ATOM    6982   C    HIS   1429     26.943  33.354  15.959  1.00  13.88
ATOM    6983   O    HIS   1429     26.383  32.525  16.704  1.00  11.14
ATOM    6984   N    MET   1430     27.286  34.566  16.348  1.00  12.42
ATOM    6985   CA   MET   1430     26.951  35.087  17.647  1.00  10.27
ATOM    6986   CB   MET   1430     28.187  35.741  18.212  1.00  11.88
ATOM    6987   CG   MET   1430     29.358  34.801  18.042  1.00  12.77
ATOM    6988   SD   MET   1430     30.824  35.317  18.863  1.00  23.27
ATOM    6989   CE   MET   1430     30.210  35.566  20.570  1.00  25.45
ATOM    6990   C    MET   1430     25.809  36.055  17.485  1.00   7.49
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Figure 23.51

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ATOM	6991	O	MET	1430	25.971	37.267	17.535	1.00	10.99
ATOM	6992	N	VAL	1431	24.641	35.475	17.250	1.00	9.86
ATOM	6993	CA	VAL	1431	23.394	36.183	17.039	1.00	9.97
ATOM	6994	CB	VAL	1431	22.229	35.166	17.026	1.00	10.82
ATOM	6995	CG1	VAL	1431	20.891	35.873	17.075	1.00	11.53
ATOM	6996	CG2	VAL	1431	22.337	34.259	15.809	1.00	8.28
ATOM	6997	C	VAL	1431	23.113	37.337	18.033	1.00	13.86
ATOM	6998	O	VAL	1431	22.727	38.431	17.606	1.00	15.08
ATOM	6999	N	PRO	1432	23.297	37.113	19.360	1.00	15.76
ATOM	7000	CD	PRO	1432	23.474	35.836	20.085	1.00	10.92
ATOM	7001	CA	PRO	1432	23.036	38.201	20.320	1.00	14.93
ATOM	7002	CB	PRO	1432	23.263	37.520	21.671	1.00	13.69
ATOM	7003	CG	PRO	1432	22.788	36.124	21.401	1.00	16.54
ATOM	7004	C	PRO	1432	23.947	39.416	20.126	1.00	13.31
ATOM	7005	O	PRO	1432	23.548	40.547	20.377	1.00	16.11
ATOM	7006	N	THR	1433	25.170	39.170	19.681	1.00	10.45
ATOM	7007	CA	THR	1433	26.122	40.229	19.430	1.00	7.78
ATOM	7008	CB	THR	1433	27.521	39.637	19.244	1.00	7.33
ATOM	7009	OG1	THR	1433	27.908	38.956	20.438	1.00	13.92
ATOM	7010	CG2	THR	1433	28.558	40.704	18.941	1.00	8.45
ATOM	7011	C	THR	1433	25.733	41.053	18.184	1.00	11.42
ATOM	7012	O	THR	1433	25.914	42.266	18.155	1.00	15.01
ATOM	7013	N	ASP	1434	25.178	40.403	17.164	1.00	10.90
ATOM	7014	CA	ASP	1434	24.835	41.087	15.920	1.00	9.93
ATOM	7015	CB	ASP	1434	24.967	40.115	14.735	1.00	10.58
ATOM	7016	CG	ASP	1434	26.350	39.494	14.653	1.00	11.03
ATOM	7017	OD1	ASP	1434	27.322	40.210	14.942	1.00	15.21
ATOM	7018	OD2	ASP	1434	26.479	38.295	14.314	1.00	15.54
ATOM	7019	C	ASP	1434	23.463	41.715	15.901	1.00	9.56
ATOM	7020	O	ASP	1434	23.286	42.793	15.373	1.00	18.13
ATOM	7021	N	LYS	1435	22.494	41.013	16.462	1.00	11.01
ATOM	7022	CA	LYS	1435	21.119	41.473	16.508	1.00	13.58
ATOM	7023	CB	LYS	1435	20.267	40.588	15.585	1.00	12.74
ATOM	7024	CG	LYS	1435	20.720	40.593	14.154	1.00	12.81
ATOM	7025	CD	LYS	1435	20.393	41.945	13.557	1.00	12.44
ATOM	7026	CE	LYS	1435	21.074	42.141	12.231	1.00	14.51
ATOM	7027	NZ	LYS	1435	20.667	43.427	11.646	1.00	8.06
ATOM	7028	C	LYS	1435	20.605	41.372	17.945	1.00	13.46
ATOM	7029	O	LYS	1435	19.766	40.501	18.248	1.00	16.10
ATOM	7030	N	PRO	1436	21.052	42.289	18.836	1.00	12.75
ATOM	7031	CD	PRO	1436	22.003	43.380	18.563	1.00	7.82
ATOM	7032	CA	PRO	1436	20.656	42.322	20.263	1.00	12.46
ATOM	7033	CB	PRO	1436	21.350	43.579	20.791	1.00	11.07
ATOM	7034	CG	PRO	1436	22.573	43.652	19.947	1.00	10.88
ATOM	7035	C	PRO	1436	19.157	42.354	20.520	1.00	11.93
ATOM	7036	O	PRO	1436	18.640	41.486	21.204	1.00	12.78

Figure 23.52

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6)   :C07K 1/14, 14/435

US CL   : 530/350, 412, 418, 421

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. :   530/350, 412, 418, 421

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
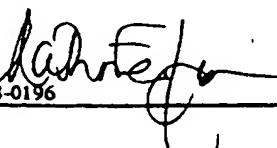
APS, STN, BIOSIS, MEDLINE, EMABSE, WPIDS

search terms: protective protein, cathepsin, crystal?,cathepsin a, ppca,rudenko, hpp

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KAZAKOVA et al. Crystallization of Cathepsin D. Biochem. Biophys. Res. Comm., 1976. Vol. 72, No. 2, pages 747-752.	1-4
A	FUSEK et al. Purification and Crystallization of Human Cathepsin D. 1992. Vol. 226, pages 555-557.	1-4
X, P	RUDENKO et al. Three-dimensional structure of the human 'protective protein': structure of the precursor form suggests a complex activation mechanism. 15 November 1995. Vol. 3, No. 11, pages 1249-1259, especially page 1257, column 1.	1-4

☐ Further documents are listed in the continuation of Box C.   ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance		
"E"	earlier document published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed	"&"	document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
14 MARCH 1997	03 APR 1997

Name and mailing address of the ISA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	CHRISTINE SAOUD
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Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US96/17325

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
   because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
   because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
   because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
   1-4

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet(1))(July 1992)*

INTERNATIONAL SEARCH REPORT

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claims 1-4, sharing the inventive concept of methods of crystallizing PPCA or pPPCA.

Group II, claims 5 and 18, sharing the inventive concept of PPCA protein.

Group III, claims 6-11, sharing the inventive concept of a method of providing an atomic model of PPCA.

Group IV, claims 12-13 and 15-16, sharing the inventive concept of a method of providing an atomic model of a ligand for PPCA.

Group V, claims 14 and 17, sharing the inventive concept of a ligand for PPCA.

The inventions listed as Groups I-V do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The claims are not so linked by a special technical feature within the meaning of PCT Rule 13.2 so as to form a single inventive concept. The "special technical features" means those technical features that define a contribution over the prior art. (See PCT Rule 13.2.) Because PPCA was known in the prior art (see description at page 1, lines 16-18), it cannot form the basis of unity of invention. Therefore, the main invention which forms a single inventive concept is Group I, claims 1-4, which is a method of crystallizing. Group II has the inventive concept of a PPCA protein, Group III has the inventive concept of a method of providing an atomic model of PPCA, Group IV had the inventive concept of providing an atomic model of a ligand for PPCA and Group V has the inventive concept of a ligand for PPCA; none of these Groups share the special technical of Group I therefore, unity of invention is lacking.